

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

Am

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>C07H 21/04, C07K 5/04, 16/00, G01N 33/53</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 00/55173</b> <b>(43) International Publication Date:</b> 21 September 2000 (21.09.00)
<b>(21) International Application Number:</b> PCT/US00/05881 <b>(22) International Filing Date:</b> 8 March 2000 (08.03.00) <b>(30) Priority Data:</b> 60/124,270 12 March 1999 (12.03.99) US <b>(71) Applicant (for all designated States except US):</b> HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Laytonsville, MD 20882 (US). <b>(74) Agents:</b> WALES, Michele, M. et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> HUMAN BREAST AND OVARIAN CANCER ASSOCIATED GENE SEQUENCES AND POLYPEPTIDES		
<b>(57) Abstract</b>  <p>This invention relates to newly identified breast, ovarian, breast cancer and/or ovarian cancer related polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "breast/ovarian cancer antigens", and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such breast/ovarian cancer antigens for detection, prevention and treatment of disorders of the female reproductive system, particularly disorders of the breast and/or ovary, including the presence of breast cancer and/or ovarian cancer. This invention relates to the breast/ovarian cancer antigens as well as vectors, host cells, antibodies directed to breast/ovarian cancer antigens and recombinant and synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing disorders related to the female reproductive system, particularly disorders of the breast and/or ovary, including breast cancer and/or ovarian cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of breast/ovarian cancer antigens of the invention. The present invention further relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.</p>		

BEST AVAILABLE COPY

*FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Larvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakistan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		



## **Human Breast and Ovarian Cancer Associated Gene Sequences and Polypeptides**

### **5    *Field of the Invention***

This invention relates to newly identified breast, ovarian, breast cancer, and ovarian cancer related polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "breast/ovarian cancer antigens," and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such  
10 breast/ovarian cancer antigens for detection, prevention and treatment of disorders of the female reproductive system, specifically disorders of the breast or ovary, particularly the presence of breast and/or ovarian cancer. This invention relates to the breast/ovarian cancer antigens as well as vectors, host cells, antibodies directed to breast/ovarian cancer antigens and recombinant and synthetic methods for producing the same. Also provided are  
15 diagnostic methods for diagnosing and treating, preventing and/or prognosing disorders related to the female reproductive system, specifically disorders of the breast and/or ovary, including breast cancer and/or ovarian cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of breast/ovarian cancer antigens of the invention. The present invention further  
20 relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.

### ***Background of the Invention***

Breast cancer represents the most frequent cause of early morbidity and mortality in  
25 women in North America (Harris et al, New Eng. J. Med. 327:319, 390 and 473 (1992)). It is generally believed that this malignancy arises from a multi step process involving mutations in a relatively small number of genes, perhaps 10 or less. These mutations result in significant changes in the growth and differentiation of breast tissue that allow it to grow independent of normal cellular controls, to metastasize, and to escape immune surveillance. The genetic  
30 heterogeneity of most breast cancers suggests that they arise by a variety of initiating events

and that the characteristics of individual cancers are due to the collective pattern of genetic changes that accumulate (Harris et al. *New Eng. J. Med.* 327:319, 390 and 473 (1992)).

The classes of genes that are involved in breast cancer are not unlike those found in a number of other well characterized malignancies, although some are highly specific for breast cancer. In particular, mutations in the genes that encode receptors involved in binding to estrogen and progesterone are particularly important because they likely cause the breast cells to proliferate while rendering them unresponsive to the antitumor effects of these hormones in advanced malignancy. In addition, changes in the genes that encode growth factors, other receptors, signal transduction molecules, and transcription factor molecules are frequently involved and have alterations that are involved in the development and progression of breast cancer (King, *Nature Genetics* 2:125 (1992)). The characterization of the type and number of mutations seen in individual breast cancers is useful in classifying the biological properties of individual cancers and in determining the prognosis for individual patients. For example, the *erbB2/HER2/neu* gene is particularly valuable in predicting the prognosis of both node-positive and node-negative patients based on the amplification status of the gene (King, *Science* 250:1684 (1990)). Several additional members of this family have been discovered but the ligand for *erbB2/HER2/neu* remains unknown. It is anticipated that further advances in therapeutics will be achieved by the development of therapies that disrupt aberrant growth signaling pathways or affect the cellular interactions of breast cancer cells with native stroma or metastatic sites.

Although oncogenes are likely to be very important in breast cancer, tumor suppressor genes may also play an important role. Certain of these genes, including p53 and Rb-1, are essential to the normal mechanisms that control cell cycle events, especially those checkpoints at the border of the different stages of the cell cycle (Hollstein et al, *Science* 253:49 (1991); Srivastava et al, *Nature* 348:747 (1990)).

In 1969, Li and Fraumeni documented a familial cancer syndrome that had an autosomal dominant pattern of expression (Li et al, *Ann. Intern. Med.* 71:747 (1969)). Members of these families had sarcomas, breast cancers, brain tumors, leukemias, adrenocortical carcinomas, and other malignancies. Family studies demonstrated that the gene responsible for the syndrome was located on chromosome 17, and examination of the p53 gene as a candidate gene revealed that this gene was mutated in five families (Malsin et al, *Science* 250:1233 (1990)). In the last two years, two genes linked to familial breast cancer,

designated BRCA1 and BRCA2, have been isolated and characterized. BRCA1 is at 17q21 (Claus et al, Am. J. Epidemiology 131:961 (1990); Hall et al, Science 250:1684 (1990); Easton et al, Am. J. of Human Genetics 52 (4):678 (1993); Black et al, Am. J. of Human Genetics 52 (4):702 (1993); Bowcock et al, Am. J. of Human Genetics 52 (4):718 (1993); Miki et al, Science 266:66 (1995)). The demonstration of loss of heterozygosity (LOH) at 17q25 has defined another potential tumor suppressor gene (Lindblom et al, Human Genetics 91:6 (1993); Cornelis et al, Oncogene 8:781 (1993); Theile et al, Oncogene 10:439 (1995)).

There is a need, therefore, for identification and characterization of such factors that modulate activation and differentiation of breast and ovarian cells, both normally and in disease states. In particular, there is a need to isolate and characterize additional molecules that mediate apoptosis, DNA repair, tumor-mediated angiogenesis, genetic imprinting, immune responses to tumors and tumor antigens and, among other things, that can play a role in detecting, preventing, ameliorating or correcting dysfunctions or diseases.

The present invention relates at least in part, to a novel breast and ovarian and breast and ovarian cancer related polynucleotides and polypeptides. The discovery of these breast and ovarian cancer related polynucleotides provides new compositions which are useful in the diagnosis, prevention and treatment of disorders of the female reproductive system, particularly of the ovary including, but not limited to ovarian cancer, and the breast, including but not limited to breast cancer.

### ***Summary of the Invention***

The present invention includes isolated nucleic acid molecules comprising, or alternatively, consisting of, a breast, ovarian, breast cancer and/or ovarian cancer associated polynucleotide sequence disclosed in the sequence listing (as SEQ ID Nos:1 to 418) and/or contained in a human cDNA clone described in Tables 1, 2 and 5 and deposited with the American Type Culture Collection ("ATCC"). Fragments, variant, and derivatives of these nucleic acid molecules are also encompassed by the invention. The present invention also includes isolated nucleic acid molecules comprising, or alternatively consisting of, a polynucleotide encoding a breast, ovarian, breast cancer, and/or ovarian cancer polypeptide. The present invention further includes breast, ovarian, breast cancer, and/or ovarian cancer polypeptides encoded by these polynucleotides. Further provided for are amino acid

sequences comprising, or alternatively consisting of, breast, ovarian, breast cancer, and/or ovarian cancer polypeptides as disclosed in the sequence listing (as SEQ ID Nos: 419 to 836) and/or encoded by a human cDNA clone described in Tables 1, 2 and 5 and deposited with the ATCC. Antibodies that bind these polypeptides are also encompassed by the invention.

5 Polypeptide fragments, variants, and derivatives of these amino acid sequences are also encompassed by the invention, as are polynucleotides encoding these polypeptides and antibodies that bind these polypeptides. Also provided are diagnostic methods for diagnosing and treating, preventing, and/or prognosing disorders related to the female reproductive system, specifically disorders related to the breast and/or ovary, including breast cancer  
10 and/or ovarian cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of breast/ovarian cancer antigens of the invention.

### *Detailed Description*

15

#### **Tables**

Table 1 summarizes some of the breast/ovarian cancer antigens encompassed by the invention (including contig sequences (SEQ ID NO:X) and the cDNA clone related to the contig sequence) and further summarizes certain characteristics of the breast/ovarian cancer  
20 polynucleotides and the polypeptides encoded thereby. The first column shows the "SEQ ID NO:" for each of the 418 breast/ovarian cancer antigen polynucleotide sequences of the invention. The second column provides a unique "Sequence/Contig ID" identification for each breast, ovarian, breast cancer and/or ovarian cancer associated sequence. The third column, "Gene Name," and the fourth column, "Overlap," provide a putative identification  
25 of the gene based on the sequence similarity of its translation product to an amino acid sequence found in a publicly accessible gene database and the database accession no. for the database sequence having similarity, respectively. The fifth and sixth columns provide the location (nucleotide position nos. within the contig), "Start" and "End", in the polynucleotide sequence "SEQ ID NO:X" that delineate the preferred ORF shown in the sequence listing as  
30 SEQ ID NO:Y. The seventh and eighth columns provide the "% Identity" (percent identity) and "% Similarity" (percent similarity), respectively, observed between the aligned sequence

segments of the translation product of SEQ ID NO:X and the database sequence. The ninth column provides a unique "Clone ID" for a cDNA clone related to each contig sequence.

Table 2 summarizes ATCC Deposits, Deposit dates, and ATCC designation numbers of deposits made with the ATCC in connection with the present application.

5 Table 3 indicates public ESTs, of which at least one, two, three, four, five, ten, fifteen or more of any one or more of these public EST sequences are optionally excluded from certain embodiments of the invention.

Table 4 lists residues comprising antigenic epitopes of antigenic epitope-bearing fragments present in most of the breast, ovarian, breast cancer or ovarian cancer associated  
10 polynucleotides described in Table 1 as predicted by the inventors using the algorithm of Jameson and Wolf, (1988) Comp. Appl. Biosci. 4:181-186. The Jameson-Wolf antigenic analysis was performed using the computer program PROTEAN (Version 3.11 for the Power MacIntosh, DNASTAR, Inc., 1228 South Park Street Madison, WI). Breast, ovarian, breast cancer and/or ovarian cancer associated polypeptides (e.g., SEQ ID NO:Y, polypeptides  
15 encoded by SEQ ID NO:X, or polypeptides encoded by the cDNA in the referenced cDNA clone) may possess one or more antigenic epitopes comprising residues described in Table 4. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly. The residues and locations shown in column two of Table 4 correspond to the amino acid sequences for most  
20 breast, ovarian, breast cancer and/or ovarian cancer associated polypeptide sequence shown in the Sequence Listing.

Table 5 shows the cDNA libraries sequenced, and ATCC designation numbers and vector information relating to these cDNA libraries.

25

### **Definitions**

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

30 In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be

"isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X (as described in column 1 of Table 1) or the related cDNA clone (as described in column 9 of Table 1 and contained within a library deposited with the ATCC). For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having an amino acid sequence encoded by a polynucleotide of the invention as broadly defined (obviously excluding poly-Phenylalanine or poly-Lysine peptide sequences which result from translation of a polyA tail of a sequence corresponding to a cDNA).

In the present invention, "SEQ ID NO:X" was often generated by overlapping sequences contained in multiple clones (contig analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X is deposited at Human Genome Sciences, Inc. (HGS) in a catalogued and archived library. As shown in column 9 of Table 1, each clone is identified by a cDNA Clone ID. Each Clone ID is unique to an individual clone and the Clone ID is all the information needed to retrieve a given clone from the HGS library. In addition to the individual cDNA clone deposits, most of the cDNA libraries from which the clones were derived were deposited at the American Type Culture Collection (hereinafter "ATCC"). Table 5 provides a list of the deposited cDNA libraries. One can use the Clone ID to determine the library source by reference to Tables 2 and 5. Table 5 lists the deposited cDNA libraries by name and links each library to an ATCC Deposit. Library names contain four characters, for example, "HTWE." The name of a cDNA clone ("Clone ID") isolated from that library begins with the same four characters, for example "HTWEP07". As mentioned below, Table 1 correlates the Clone ID names with SEQ ID NOs. Thus, starting with a SEQ ID NO, one can use Tables 1, 2 and 5 to determine the corresponding Clone ID, from which library it came and in which ATCC deposit the library is contained. Furthermore,

it is possible to retrieve a given cDNA clone from the source library by techniques known in the art and described elsewhere herein. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposits were made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for the purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, or the complement thereof (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein), and/or sequences contained in the related cDNA clone within a library deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65 degree C.

Also included within "polynucleotides" of the present invention are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH<sub>2</sub>PO<sub>4</sub>; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50 degree C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA<sup>+</sup> sequences (such as any 3' terminal polyA<sup>+</sup> tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

The polynucleotides of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

"SEQ ID NO:X" refers to a breast/ovarian cancer antigen polynucleotide sequence described in Table 1. SEQ ID NO:X is identified by an integer specified in column 1 of Table 1. The polypeptide sequence SEQ ID NO:Y is a translated open reading frame (ORF)



encoded by polynucleotide SEQ ID NO:X. There are 418 breast/ovarian cancer antigen polynucleotide sequences described in Table 1 and shown in the sequence listing (SEQ ID NO:1 through SEQ ID NO:418). Likewise there are 418 polypeptide sequences shown in the sequence listing, one polypeptide sequence for each of the polynucleotide sequences (SEQ ID NO:419 through SEQ ID NO:836). The polynucleotide sequences are shown in the sequence listing immediately followed by all of the polypeptide sequences. Thus, a polypeptide sequence corresponding to polynucleotide sequence SEQ ID NO:1 is the first polypeptide sequence shown in the sequence listing. The second polypeptide sequence corresponds to the polynucleotide sequence shown as SEQ ID NO:2, and so on. In other words, since there are 418 polynucleotide sequences, for any polynucleotide sequence SEQ ID NO:X, a corresponding polypeptide SEQ ID NO:Y can be determined by the formula  $X + 418 = Y$ . In addition, any of the unique "Sequence/Contig ID" defined in column 2 of Table 1, can be linked to the corresponding polypeptide SEQ ID NO:Y by reference to Table 4.

The polypeptides of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation,

hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

The breast, ovarian, breast cancer and/or ovarian cancer polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The breast, ovarian, breast cancer and/or ovarian cancer polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to

a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

"A polypeptide having functional activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular assay, such as, for example, a biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention).

The functional activity of the breast/ovarian cancer antigen polypeptides, and fragments, variants derivatives, and analogs thereof, can be assayed by various methods.

For example, in one embodiment where one is assaying for the ability to bind or compete with full-length polypeptide of the present invention for binding to an antibody to the full length polypeptide antibody, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See

generally, Phizicky, E., et al., Microbiol. Rev. 59:94-123 (1995). In another embodiment, physiological correlates polypeptide of the present invention binding to its substrates (signal transduction) can be assayed.

5 In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present invention and fragments, variants derivatives and analogs thereof to elicit polypeptide related biological activity (either in vitro or in vivo). Other methods will be known to the skilled artisan and are within the scope of the invention.

10

**Breast, Ovarian, Breast Cancer and Ovarian Cancer Associated Polynucleotides and Polypeptides of the Invention**

15 It has been discovered herein that the polynucleotides described in Table 1 are expressed at significantly enhanced levels in human breast, ovarian, breast cancer and/or ovarian cancer tissues. Accordingly, such polynucleotides, polypeptides encoded by such polynucleotides, and antibodies specific for such polypeptides find use in the prediction, diagnosis, prevention and treatment of disorders related to the female reproductive system, specifically disorders of the breast and/or ovary, including breast cancer and/or ovarian cancer as more fully described below.

20 Table 1 summarizes some of the polynucleotides encompassed by the invention (including contig sequences (SEQ ID NO:X) and the related cDNA clones) and further summarizes certain characteristics of these breast, ovarian, breast cancer and/or ovarian cancer associated polynucleotides and the polypeptides encoded thereby.

Table 1

Seq ID No.	Sequence/Contig ID	Gene Name	Overlap	HGS Nucleotide		% Identity	% Similarity	Clone ID
1	419266	monoamine oxidase B [Homo sapiens] >gij187376 monoamine oxidase B [Homo sapiens] >bbs1134021 monoamine oxidase B, MAO B [human, platelet, Peptide Partial, 520 aa] [Homo sapiens] >pirJH0817JH0817 amine oxidase (flavin-containing) (EC 1.4.3.4) B - human >	gij187359	Start	End	95	95	HAGFP75
2	429114			51	383			HATDC43
3	506777			51	233			HRGCY74
4	508678	(AF059293) cytokine-like factor-1 precursor [Homo sapiens] >sp O75462 O75462 CYTOKINE-LIKE FACTOR-1 PRECURSOR. Length = 422	gij3372627	3	155	100	100	HFIJG81
5	508968	DNA helicase [Homo sapiens] >pir A58836 A58836 DNA helicase RECQL - human Length = 659	gij619863	2	739	95	96	HHTLH91
6	509029			770	1096			HLMDG72
7	519726			359	529			HCSSB83

8	522632		3	299		HRGBG45
9	524655		522	686		HUSGS36
10	525847	glyoxalase II [Homo sapiens] >sp Q16775 GLO2_HUMAN HYDROXYACYLGLUTATHIONE HYDROLASE (EC 3.1.2.6) (GLYOXALASE II) (GLX II). Length = 260	1	162	54	73 H6EDP14
11	530306		239	355		HCHCC28
12	532818	(AF035178) elongation factor 1 A2 [Oryctolagus cuniculus] >gi 38456 elongation factor 1 alpha-2 [Homo sapiens] >pir S35033 EFHUA2 translation elongation factor eEF-1 alpha-2 chain - human >sp Q05639 EF12_HUMAN ELONGATION FACTOR 1-ALPHA 2 (EF-1-ALPHA-2) (S	43	441	95	95 HAMFD92
13	533385		1258	1827		HTWAO42
14	533532	actin capping protein alpha subunit [Homo sapiens] >gi 2393732 (AC002543) f-actin capping protein alpha-2 subunit [Homo sapiens] >sp P47755 CAZ2_HUMAN F- ACTIN CAPPING PROTEIN ALPHA-2 SUBUNIT (CAPZ). >gi 433308 capping protein alpha [Homo sapiens] {SUB 3-2	18	947	95	95 HETCD42

15	534852	(AF041472) ataxin-2 [Mus musculus] >sp O70305 O70305 SPINOCEREBELLAR ATAXIA 2 HOMOLOG (ATAXIN-2). Length = 1285 R kappa B [Homo sapiens] >pir S52863 S52863 DNA-binding protein R kappa B - human >sp Q15312 Q15312 R KAPPA B. Length = 1324	gil3005020	3	869	77	77	HCE4Q55
16	537910		gil695579	3	443	100	100	HTOAO52
17	538460			574	1026			HSSMY42
18	539577	transcriptional activator [Homo sapiens] >gnl PID d1005685 HSNF2b [Homo sapiens] >pir S45252 S45252 SNF2beta protein - human >gil4056413 (AC006127) SN24_HUMAN; nuclear protein GRB1; homeotic gene regulator; SNF2-BETA [Homo sapiens] {SUB 814-1474} Length =	gil902046	1	540	89	89	HKADQ93
19	548379	complement protein C7 precursor [Homo sapiens] >pir A27340 A27340 complement C7 precursor - human >sp P10643 CO7_HUMAN COMPLEMENT COMPONENT C7 PRECURSOR. Length = 843 proteasome subunit HsN3 [Homo sapiens] >pir S50147 S50147 multicatalytic endopeptidase complex (EC 3.4.99.46) beta chain N3 - human >sp P28070 PRCB_HUMAN PROTEASOME BETA CHAIN PRECURSOR (EC 3.4.99.46) (MACROPAIN BETA CHAIN)	gil179716	92	1336	92	92	HATCK25
20	548489		gnl PID d100 6192	3	857	99	99	HCGAF33

(MULTICATALYTIC ENDOPEPTIDASE  
C

21	548595	inosine monophosphate dehydrogenase type II [Homo sapiens] >gi 1702964 inosine monophosphate dehydrogenase type II [Homo sapiens] >pir 52303 A31997 IMP dehydrogenase (EC 1.1.1.205) II - human >sp P12268 IMD2_HUMAN INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE	gi 602458	971	1525	100	100	HTXEE92
22	549337	stromelysin-3 precursor [Homo sapiens] Length = 488	gi 456257	449	1081	96	96	HJMAF23
23	549777			54	293			HPMAC61
24	553091	pancreatic peptidylglycine alpha-amidating monooxygenase, PAM=membrane-bound isoform {alternatively spliced, clone PAM-3, transmembrane domain (Ba region)} [human, islet cell tumor cell line QGP-1, Peptide Partial, 971 aa] [Homo sapiens] >sp Q16252 Q16252	bbs 159681	898	2598	97	97	HEMFU73
25	553827	B-CAM gene product [Homo sapiens] >pir 37202 37202 B-CAM protein - human Length = 588	gi 535179	2	388	80	80	HIBHMI67



26	556350		263	655		HCHOC59		
27	556351	'FKBP52; 52 kD FK506 binding protein' [Homo sapiens] >pir A46372 A46372 immunophilin FKBP52 - human >sp Q02790 FKB4_HUMAN P59 PROTEIN (HSP BINDING IMMUNOPHILIN) (HBI) (POSSIBLE PEPTIDYL-PROLYL CIS-TRANS ISOMERASE) (EC 5.2.1.8) (PPIASE) (ROTAMASE) (FKBP5 ubiquitin conjugating enzyme [Homo sapiens] >pir A49630 A49630 ubiquitin conjugating enzyme - human (fragment) Length = 298 (AD001530) putative [Homo sapiens] >sp G2335055 G2335055 XAP-5. >gnl PID d1012538 HXC-26 [Homo sapiens] {SUB 15-339} >gij 203974 XAP-5 gene product [Homo sapiens] {SUB 66-339} Length = 339 adipocyte lipid-binding protein [Homo sapiens] >pir A33363 FZHU fatty acid-binding protein, adipocyte - human >sp P15090 FABA_HUMAN FATTY ACID-BINDING PROTEIN, ADIPOCYTE (AFABP) (ADIPOCYTE LIPID-BINDING PROTEIN) (ALBP) (A-FABP). {SUB 2-132} Length = 132 N-cadherin [Homo sapiens] Length = 747	gij 186390	2	1216	97	HE8DF57	
28	557007		gij 388309	3	698	99	100	HTEJK85
29	558140		gij 2335055	3	1070	71	71	HKAAM18
30	558456		gij 178347	69	332	100	100	HISBQ67
31	558708		gij 416293	3	515	79	79	HSYBX61
32	574789			301	402			HLDNM79

33	578203		2	445		H6EDN57
34	585385	precursor polypeptide (AA -21 to 782) [Homo sapiens] >pir A35954 A35954 endoplasmic precursor - human >sp P14625 ENPL_HUMAN ENDOPLASMIN PRECURSOR (94 KD GLUCOSE-REGULATED PROTEIN) (GRP94) (GP96 HOMOLOG) (TUMOR REJECTION ANTIGEN 1). Length = 803 leukocyte adhesion glycoprotein precursor [Homo sapiens] Length = 1152	99	347	71	IIQI'MI'70
35	588869		1	720	98	HDPFK39
36	597076	preferentially expressed antigen of melanoma [Homo sapiens] >sp P78395 P78395 PREFERENTIALLY EXPRESSED ANTIGEN OF MELANOMA. Length = 509 sigma receptor [Homo sapiens] >gil 916800 SR31747 binding protein 1 [Homo sapiens] >gil 2914740 (AF001977) type I sigma receptor [Homo sapiens] >pir JC5266 JC5266 sigma receptor 1 - human >sp Q99720 Q99720 SIGMA RECEPTOR. Length = 223	80	811	77	HEETHE66
37	598656		3	587	100	HMEIY05

38	611880	Acetyl-CoA:acetyltransferase (EC 2.3.1.9) (Acetoacetyl-CoA thiolase). [Escherichia coli] >gil1788554 (AE000311) acetyl-CoA acetyltransferase [Escherichia coli] >pir F64992 F64992 hypothetical protein b2224 - Escherichia coli (strain K-12) >sp P76461 ATOB_	gn PID d1016745	1	108	100	100	HOVAS88
39	614329	ORF, HEIR-1; pot. neuroblastoma-associated regulator [Homo sapiens] >gil395338 helix-loop-helix protein [Homo sapiens] >gil512437 HEIR-1 [Homo sapiens] {SUB 30-148} Length = 148	gil490013	300	755	86	86	HFPCQ02
40	616066			121	213			HSIGC05
41	620956	ribosomal protein S9 [Rattus norvegicus] >pir JN0587 S21497 ribosomal protein S9 - rat Length = 194	gil57143	3	473	95	97	HOFOB28
42	621889	unnamed protein product [unidentified] >gil468550 CCT (chaperonin containing TCP-1) epsilon subunit [Mus musculus] >pir S43061 S43061 t-complex-type molecular chaperone Ccte - mouse Length = 541	gn PID c306129	16	423	95	97	HOFOC44
43	624017	(AB003732) polyubiquitin [Cricetulus griseus] >sp O35080 O35080 POLYUBIQUITIN. >gil4105408 (AF045474) polyubiquitin [Schistosoma mansoni] {SUB 694-988} Length = 1038	gil2627133	1	1170	95	97	HMCBS12

44	651784	histone H2A.X [Homo sapiens] >pir S07631 S07631  histone H2A.X - human >sp P16104 H2AX_HUMAN HISTONE H2A.X. {SUB 2-143} Length = 143	gi 31973	2	514	98	98	HKGA194
45	651826	keratin, 55K type II cytoskeletal - human (fragment) Length = 489	pir B24177 B 24177	2	1300	86	86	HNTAH42
46	653282	phosphate transfer protein B precursor, mitochondrial - bovine Length = 361	pir D53737 D 53737	30	392	90	90	HOFNY90
47	657122			1	204			HKGAQ13
48	661442	rab1B protein (AA 1 - 201) [Rattus sp.] Length = 201	gi 57006	1	672	98	99	HICHMI33
49	664914	phosphotyrosyl phosphatase activator [Oryctolagus cuniculus] >pir B54021 B54021 phosphotyrosyl phosphatase activator PTPA - rabbit >sp Q28717 Q28717 PHOSPHOTYROSYL PHOSPHATASE ACTIVATOR. Length = 323	gi 509144	1	228	98	100	HEGAK11
50	666654			63	395			HOFNL37
51	667084	cytokeratin 17 [Homo sapiens] >gi 34075 keratin related product [Homo sapiens] >pir S30433 S30433 keratin 17, cytoskeletal - human >sp Q04695 K1CQ_HUMAN KERATIN, TYPE I CYTOSKELETAL 17 (CYTOKERATIN 17) (K17) (CK 17) (39.1) (VERSION 1). {SUB 2-432} Length	gi 30379	3	1379	100	100	HKADA74

52	667380	cell surface glycoprotein [Homo sapiens] >gnl PID d1006754 TALLA-1 [Homo sapiens] >gnl PID d1001976 cell surface glycoprotein [Homo sapiens] >pir 39368 39368 T-cell acute lymphoblastic leukemia associated antigen 1 - human >sp P41732 A15_HUMAN CELL SURF	gnl PID d1001976	1	474	100	100	HMIBK53
53	669530			264	440			HPFCJ30
54	671315	cell cycle checkpoint control protein [Homo sapiens] >sp Q99638 Q99638 CELL CYCLE CHECKPOINT CONTROL PROTEIN. Length = 391	gij 765956	320	1279	92	92	HIDABE95
55	671993	NAD(H)-specific isocitrate dehydrogenase gamma-subunit precursor [Homo sapiens] >gnl PID e219959 NAD (H)-specific isocitrate dehydrogenase gamma subunit precursor [Homo sapiens] >gij 302655 NAD+-isocitrate dehydrogenase gamma subunit [Homo sapiens] >gij 40	gnl PID e211919	1	993	91	91	HSJCA89
56	674618			223	312			HOVBX22
57	675027			789	1160			HSDII69
58	677202	vimentin [Homo sapiens] >sp Q15867 Q15867 VIMENTIN (FRAGMENT). Length = 354	gij 340232	705	896	100	100	HWACG51

59	678504	ORF YGR031w [Saccharomyces cerevisiae] >pir S64322 S64322 probable membrane protein YGR031w - yeast (Saccharomyces cerevisiae) Length = 342	gnl PID e2432 77	320	640	38	63	HCHAG27
60	678985	54 kDa protein [Homo sapiens] >gnl PID e1245514 p54nrb [Homo sapiens] >pir G01211 G01211 54 kDa protein - human >sp Q12786 Q12786 54 KDA PROTEIN. Length = 471 (AF036241) Na+/H+ exchange regulatory co-factor [Homo sapiens] >gi 3220019 (AF015926) ezrin-radixin-moesin binding phosphoprotein-50 [Homo sapiens] >sp O14745 O14745 EZRIN-RADIXIN-MOESIN BINDING PHOSPHOPROTEIN-50. Length = 358	gi 407308	358	1203	100	100	HCHOL54
61	682161	(AF036241) Na+/H+ exchange regulatory co-factor [Homo sapiens] >gi 3220019 (AF015926) ezrin-radixin-moesin binding phosphoprotein-50 [Homo sapiens] >sp O14745 O14745 EZRIN-RADIXIN-MOESIN BINDING PHOSPHOPROTEIN-50. Length = 358	gi 2920585	3	869	89	89	HCHAG19
62	683476	KDEL receptor [Homo sapiens] >pir S13293 S13293 KDEL receptor - human >sp P24390 P24390 HUMAN ER LUMEN PROTEIN RETAINING RECEPTOR 1 (KDEL RECEPTOR 1). Length = 212	gi 34031	1	132	100	100	HOFMM27
63	691146	KDEL receptor [Homo sapiens] >pir S13293 S13293 KDEL receptor - human >sp P24390 P24390 HUMAN ER LUMEN PROTEIN RETAINING RECEPTOR 1 (KDEL RECEPTOR 1). Length = 212	gi 34031	1	372	100	100	IIDAB02
64	693589	KDEL receptor [Homo sapiens] >pir S13293 S13293 KDEL receptor - human >sp P24390 P24390 HUMAN ER LUMEN PROTEIN RETAINING RECEPTOR 1 (KDEL RECEPTOR 1). Length = 212	gi 34031	1	393	100	100	HCHAS12

65	694991	B4B gene product [Homo sapiens] >gnl PID e265628 progression associated protein [Homo sapiens] >gj 1932786 epithelial membrane protein [Homo sapiens] >gj 2506160 TMP [Homo sapiens] >sp P54849 EMPI_HUMAN EPITHELIAL MEMBRANE PROTEIN-1 (EMP-1) (TUMOR-ASSOCIA	gnl PID e1949 46	1	663	98	98	HRAAY77
66	698303	heat shock factor 1 [Homo sapiens] >pir A41137 A41137 heat shock transcription factor 1 - human >sp Q00613 HSF1_HUMAN HEAT SHOCK FACTOR PROTEIN 1 (HSF 1) (HEAT SHOCK TRANSCRIPTION FACTOR 1) (HSTF 1). Length = 529 filamin [Homo sapiens] Length = 2647	gj 184403	23	1168	85	85	HSHCASS
67	698669		gj 1203969	27	1274	98	98	HEGAR20
68	705696			321	458			HOFMP28
69	706393	vacuolar H+ ATPase proton channel subunit [Homo sapiens] >pir A39367 A39367 H+- transporting ATPase (EC 3.6.1.35) chain PKD1 - human Length = 155	gj 189676	119	604	84	85	HSKHIP64
70	707357			3	344			HOFMM35

71	707360	leucine aminopeptidase, LAP [cattle, kidney, Peptide, 513 aa] [Bos taurus] >pir A54338 APBOL leucyl aminopeptidase (EC 3.4.11.1), renal - bovine >sp P00727 AMPL_BOVIN CYTOSOL AMINOPEPTIDASE (EC 3.4.11.1) (LEUCINE AMINOPEPTIDASE) (LAP) (LEUCYL AMINOPEPTIDASE)	bbs 137417	1	447	81	89	HOFOF35
72	707375	serine/threonine protein kinase [Homo sapiens] >pir S23385 S23385 protein kinase (EC 2.7.1.37) cdc2-related PCTAIRE-1 - human >sp Q00536 KPT1_HUMAN SERINE/THREONINE-PROTEIN KINASE PCTAIRE-1 (EC 2.7.1.-). >sp G252370 G252370 CDC2-RELATED PROTEIN KINASE {CL	gi 36619	2	1582	92	92	HTOJQ73
73	707754			2	376			HLDBT45
74	711172			237	395			HOVC140
75	712248	transcription factor AP-2 beta [Homo sapiens] >sp E286536 E286536 TRANSCRIPTION FACTOR AP-2 BETA. Length = 367	gnl PID e286536	99	344	100	100	HKG CW94
76	715445	DNA-PK [Homo sapiens] >pir G02083 G02083 DNA-PK - human (fragment) >sp Q13337 Q13337 DNA-PK (FRAGMENT). Length = 930	gi 1017757	119	988	99	99	HL1DJ07
77	716362			221	688			HIBGBC77



78	716835	(AF036241) Na+/H+ exchange regulatory co-factor [Homo sapiens] >gi 3220019 (AF015926) ezrin-radixin-moesin binding phosphoprotein-50 [Homo sapiens] >sp O14745 O14745 EZRIN-RADIXIN-MOESIN BINDING PHOSPHOPROTEIN-50. Length = 358	gi 2920585	3	755	79	79	HCHAI81
79	716947	SRp55-2 [Homo sapiens] Length = 135	gi 1049084	2	145	100	100	HADDY71
80	717685	alpha-mannosidase [Homo sapiens] Length = 987	gi 1419374	2	1120	99	99	HIDPUOIS
81	719755			89	802			HCGAC54
82	720389	inducible membrane protein [Homo sapiens] >gi 806806 cell surface glycoprotein [Homo sapiens] >gi 1832296 metastasis suppressor [Homo sapiens] >pir 138942/A46493 metastasis suppressor KAI1 - human >sp P27701 CD82_HUMAN CD82 ANTIGEN (INDUCIBLE MEMBRANE PRO	gi 35833	1	594	65	67	HUVCR41
83	720903	cDNA isolated for this protein using a monoclonal antibody directed against the p27k prosomal protein [Homo sapiens] Length = 266	gnl P1D e103161	108	614	93	95	HFV1H35

84	721348	G6PD (AA 1-515) [Homo sapiens] >sp P11413 G6PD_HUMAN GLUCOSE-6-PHOSPHATE 1-DEHYDROGENASE (EC 1.1.1.49) (G6PD). {SUB 2-515} >gi 439445 glucose-6-phosphate dehydrogenase [Didelphis virginiana] {SUB 258-288} >sp O46666 O46666 GLUCOSE-6-PHOSPHATE DEHYDROGENAS	gi 31543	545	2065	93	93	HSHBL14
85	721562	pescadillo [Homo sapiens] >sp O00541 O00541 PESCADILLO. Length = 588	gi 2194203	32	811	99	99	HCFCCK84
86	722775			409	1680			HCHAD52
87	724463			126	335			HOFMP50
88	727501	SWI/SNF complex 170 KDa subunit [Homo sapiens] >sp Q92923 Q92923 SWI/SNF COMPLEX 170 KDA SUBUNIT. Length = 1213	gi 1549241	1	1302	97	97	HL YBV46
89	728418	GTP binding protein [Mus musculus] >pir A39611 A39611 probable GTP-binding protein - mouse >sp P23249 MV10_MOUSE PROTEIN MOV-10. >gi 433685 gb 110 /Mov 10 locus gene product [Mus musculus] {SUB 1-45} Length = 1004	gi 53169	3	911	93	96	HSSEP09
90	728920	adipophilin [Homo sapiens] >sp Q99541 Q99541 ADIPOPHILIN (FRAGMENT). Length = 437	gnl PID e292752	2	751	89	89	HILDRQ71
91	732958			3	296			HPTYA52

92	733134	NF45 protein [Homo sapiens] >pir A54857 A54857 transcription factor NF-AT 45K chain - human >sp Q12905 Q12905 NF45 PROTEIN. Length = 406	gi 532313	84	1259	100	100	HHBHP80
93	734099			150	365			HBGDI44
94	734599			163	705			H6EED05
95	736019	ribosomal protein L11 [Homo sapiens] >gi 57678 ribosomal protein L11 [Rattus rattus] >pir S17351 RSRT11 ribosomal protein L11 precursor - rat >sp G3115334 G3115334 RIBOSOMAL PROTEIN L11. >sp D1026769 D1026769 RIBOSOMAL PROTEIN L11 (FRAGMENT). {SUB 17-52}	gi 3115334	3	608	100	100	HSEBB02
96	738268			45	233			HE2OC41
97	738911	(AF069291) hT41 [Homo sapiens] >sp G3687829 G3687829 HT41. Length = 505	gi 3687829	3	656	40	62	HCHCI12
98	739226			3	125			HADFY59
99	739527			3	752			HACCL62
100	740710	acyl-CoA synthetase-like protein [Homo sapiens] Length = 670	gn P1D1e3212 96	8	307	96	100	HPMFQ72

101	742980	serine-threonine specific protein phosphatase [Homo sapiens] >sp E1334695 E1334695 SERINE-THREONINE SPECIFIC PROTEIN PHOSPHATASE (EC 3.1.3.16). Length = 317	gnl PID e1334695	3	182	81	86	HSKCE51
102	744331	ZINC FINGER PROTEIN {N-TERMINAL}. Length = 77	sp G632682 G632682	432	791	62	80	HCHAH75
103	744751	collagen alpha 3(VI) chain precursor - human Length = 2970	pir S13679 C GHU3A	902	1189	100	100	HUJFFV63
104	745750			349	714			HCEHX66
105	746285			2016	2297			HNTNQ78
106	746416	(AB013357) 49 kDa zinc finger protein [Mus musculus] Length = 460	gnl PID J1038083	113	391	97	97	HOFMO90
107	747851	(AF035387) C7-1 protein [Rattus norvegicus] >sp O54715 O54715 C7-1 PROTEIN. Length = 463	gi 2655418	3	974	78	80	HSSJG21
108	750632			252	449			HOGBF68
109	751315			423	608			HLTGN10
110	754009			408	773			HE8PN81
111	754634			525	1070			HUSGH70
112	756637	(AF044127) peroxisomal short-chain alcohol dehydrogenase [Homo sapiens] >sp G4105190 G4105190 PEROXISOMAL SHORT-CHAIN ALCOHOL DEHYDROGENASE. Length = 260	gi 4105190	38	586	89	91	HMWY27

113	756833		1	387		HCEDP17	
114	756878		127	399		IIBDE92	
115	757332	cytokeratin 8 [Homo sapiens] >gi 553163 keratin 8 [Homo sapiens] {SUB 1-231} Length = 482	35	235	96	100	HOFMI52
116	760835	Pectinase gene transcriptional regulator. [Escherichia coli] >gnl PID d1015936 Pectinase gene transcriptional regulator. [Escherichia coli] >gi 1787806 (AE000250) putative transcriptional regulator LYSR- type [Escherichia coli] >pir A64907 A64907 hypotheti	3	434	100	100	HE9BW44
117	761760	F45G2.10 [Caenorhabditis elegans] >sp O62252 O62252 F45G2.10 PROTEIN. Length = 160	3	527	61	81	HMWIF41
118	762520	B-myb protein (AA 1-700) [Homo sapiens] >pir S0199 S0199 transforming protein B-myb - human >sp P10244 MYBB_HUMAN MYB- RELATED PROTEIN B (B-MYB). Length = 700	77	520	100	100	HBJJIB76
119	764461		2	211			HOFMH95
120	764517	phosphomevalonate kinase [Homo sapiens] >sp Q15126 PMKA_HUMAN PHOSPHOMEVALONATE KINASE (EC 2.7.4.2) (PMKASE). {SUB 2-192} >gi 3445542 (AF026069) phosphomevalonate kinase [Homo sapiens] {SUB 33-192} Length = 192	260	877	100	100	HCGAA73

121	765132	clk1; putative [Homo sapiens] >pir S53641 S53641 protein kinase clk1 (EC 2.7.1.-) - human >sp P49759 CLK1_HUMAN PROTEIN KINASE CLK1 (EC 2.7.1.-) (CLK). Length = 484	gij632964	1202	2251	99	99	HE9QA05
122	765667	(AF043250) mitochondrial outer membrane protein [Homo sapiens] >gij3941347 (AF043253) mitochondrial outer membrane protein [Homo sapiens] >gij4105703 (AF050154) D19S1177E [Homo sapiens] >sp G3941342 G3941342 MITOCHONDRIAL OUTER MEMBRANE PROTEIN. >sp G3941	gij3941342	144	1115	91	91	HCHOB54
123	767113	putative progesterone binding protein [Homo sapiens] >sp O00264 O00264 PUTATIVE PROGESTERONE BINDING PROTEIN. Length = 195	gnl PID e3141 74	66	677	93	93	HNTMW26
124	767204	cytochrome P450IIC4 [Oryctolagus cuniculus] >pir S20227 S20227 cytochrome P450 2C4 - rabbit (fragment) >sp Q29507 Q29507 CYTOCHROME P450 (EC 1.14.14.1) (FRAGMENT). Length = 145	gij164933	3	581	43	61	HCHIAN75
125	767400			2	1057			HSYBI74

126	767962	proteasome subunit C3 [Homo sapiens] >pir S15970 SNHUC3 multicatalytic endopeptidase complex (EC 3.4.99.46) chain C3 - human >sp P25787 PRC3_HUMAN PROTEASOME COMPONENT C3 (EC 3.4.99.46) (MACROPAIN SUBUNIT C3) (MULTICATALYTIC ENDOPEPTIDASE COMPLEX SUBUNIT (AB002086) p47 [Rattus norvegicus] >gn PID e294068 XY40 protein [Rattus norvegicus] >sp O35987 O35987 P47, COMPLETE CDS. Length = 370 adenine phosphoribosyltransferase [Homo sapiens] >gi 28819 adenine phosphoribosyltransferase (aprt) [Homo sapiens] >pir S06232 RTHUA adenine phosphoribosyltransferase (EC 2.4.2.7) - human >sp P07741 APT_HUMAN ADENINE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.7)	gn PID d100 1115	3	722	100	100	HABAF63
127	768040		gn PID d102 2509	119	661	84	89	HSRDI53
128	769956		gi 178867	2	592	100	100	HUFFC71
129	770133			958	1236			HUSAX93
130	770289	ALDH7 [Homo sapiens] >pir I38669 I38669 ALDH7 - human >sp P43353 DHA7_HUMAN ALDEHYDE DEHYDROGENASE 7 (EC 1.2.1.5). >sp G601780 G601780 ALDH7. Length = 468	gi 601780	194	340	65	69	HCHAO38

131	771964	(AD000092) human RAD23A homolog [Homo sapiens] >gnl PID d1005299 HHR23A protein [Homo sapiens] >pir S44443 S44443 RAD23 protein homolog2 - human Length = 363 B-myb protein (AA 1-700) [Homo sapiens] >pir S01991 S01991 transforming protein B-myb - human >sp P10244 MYBB_HUMAN MYB- RELATED PROTEIN B (B-MYB). Length = 700	gi 1905912	29	1165	76	76	HAMGD77
132	772582	zinc finger protein [Homo sapiens] >pir I38620 I38620 zinc finger protein ZNF155 - human (fragment) Length = 139	gi 29472	150	974	99	99	HYAAO51
133	773387	novel serine protease, PRSS11 [Homo sapiens] >gnl PID d1014012 serin protease with IGF-binding motif [Homo sapiens] >sp Q92743 Q92743 NOVEL SERINE PROTEASE, Length = 480 protein of unknown function [Homo sapiens] >pir C35826 C35826 hypothetical protein A, 13K - human >sp Q00994 HG74_HUMAN OVARIAN GRANULOSA CELL 13.0 KD PROTEIN HGR74. Length = 111	gi 495576	152	634	46	64	HAIJBC78
134	773827		gnl PID e2751 86	3	1217	100	100	HKAD115
135	774108		gi 189379	303	623	75	75	HEGAC01



136	774636	glutathione transferase [Homo sapiens] >pir A39375 A39375 glutathione transferase (EC 2.5.1.18) class mu, GSTM2 - human >sp P28161 GTM2_HUMAN GLUTATHIONE S-TRANSFERASE MU 2 (EC 2.5.1.18) (GSTM2-2) (CLASS-MU). {SUB 2-218} >gnl PID e33921 glutathione transf	gi 183301	61	747	98	98	HISDV78
137	775339	SWI/SNF complex 60 KDa subunit [Homo sapiens] >sp Q92924 Q92924 SWI/SNF COMPLEX 60 KDA SUBUNIT. Length = 435	gi 1549243	3	320	98	100	HSIGB35
138	775582			448	705			HIEPNB30
139	775779	(AJ000332) Glucosidase II [Homo sapiens] >sp Q14697 Q14697 GLUCOSIDASE II PRECURSOR (K1AA0088). >gnl PID d1008224 The ha1225 gene product is related to human alpha- glucosidase. [Homo sapiens] {SUB 2-944} Length = 944	gnl PID e3281 43	1	1695	98	98	HLWAS86
140	777809	cysteine-rich protein 2 [Homo sapiens] >gnl PID d1008288 ESP1/CRP2 [Homo sapiens] >pir G02090 G02090 cysteine-rich protein 2 - human >sp P52943 CRP2_HUMAN CYSTEINE- RICH PROTEIN 2 (CRP2) (ESP1 PROTEIN). Length = 208	gi 1399028	202	681	99	100	HSPMB57
141	778927	valyl-tRNA synthetase [Homo sapiens] >pir S17675 S17675 valine--tRNA ligase (EC 6.1.1.9) - human Length = 1265	gi 31545	1843	3282	88	88	HMVVBW39

142	779262		1	288			HTENK29
143	779392		2	181			HE2FO87
144	780149	proteasome activator hPA28 suunit beta [Homo sapiens] >pir I53518 I53518 proteasome activator hPA28 suunit beta - human >sp Q15129 Q15129 PROTEASOME ACTIVATOR HPA28 SUUNIT BETA. >sp G693763 G693763 PA28=REGULATORS OF THE 20 S PROTEASOME {PEPTIDE 15}. {SUB	233	955	93	93	HSPMF83
145	780583		8	607			HHIEW04
146	780960		232	576			HOEBN65
147	781469	radixin [Homo sapiens] >pir A46127 A46127 radixin - human Length = 583	1	303	100	100	HNTRA25
148	781556		116	190			HOSAW82
149	781771		1	822			HE6EO05
150	782033	histone H2A [Gallus gallus] Length = 129	146	544	98	100	HULCC66
151	782105		606	1064			HKAKV16

152	782122	high density lipoprotein binding protein [Homo sapiens] >pir A44125 A44125 high density lipoprotein-binding protein, 110K - human >sp Q00341 HBP_HUMAN HIGH DENSITY LIPOPROTEIN BINDING PROTEIN (HDL-BINDING PROTEIN). >sp G1478463 G1478463 VIGILIN=KH PROTEIN	gj 183892	3	983	95	95	HSRAB32
153	783135	zinc finger protein [Homo sapiens] >sp O00488 O00488 ZINC FINGER PROTEIN. Length = 116	gn P1D1d102 1201	3	500	97	99	HCHCB61
154	783245			3	341			HTSFV77
155	783247			95	391			HBMGMD18
156	783413	D9 splice variant 3 [Mus musculus] >sp O08695 O08695 D9 SPLICE VARIANT 3. Length = 169	gj 2071991	1	591	80	88	HEBFR23
157	784407			45	185			HFKAA09
158	784548	nuclear RNA helicase (DEAD family) [Homo sapiens] >pir I37201 I37201 nuclear RNA helicase (DEAD family) BAT1 - human >sp Q13838 HE47_HUMAN PROBABLE ATP-DEPENDENT RNA HELICASE P47. >gj 2739119 (AF029061) BAT1 [Homo sapiens] {SUB 145-428} >gj 971677 express	gj 587146	676	1020	90	92	HSRFZ85

159	785075	KIAA0100 is a human counterpart of mouse e1 gene. [Homo sapiens] >sp Q14667 Q14667 KIAA0100 (HUMAN COUNTERPART OF MOUSE E1 GENE). Length = 2092	gnl PID d100 8477	72	1109	93	93	HDPFX40
160	785677	(AC004084) similar to DNA-DIRECTED RNA POLYMERASE II 13.3 KD POLYPEPTIDE; 98% similar to P5243 (PID:g I710661) [Homo sapiens] >sp O43375 O43375 SIMILAR TO DNA-DIRECTED RNA POLYMERASE II 13.3 KD POLYPEPTIDE (FRAGMENT). Length = 105	gi 2822158	1	273	95	100	HBSAJ50
161	786238			2	994			HOVCA75
162	786389			3	1124			ILLJDU61
163	786929	(AJ224442) methyltransferase [Homo sapiens] >sp O43709 O43709 METHYLTRANSFERASE. Length = 220 PIPPin protein [Rattus norvegicus] >pir JC4588 JC4588 RNA-binding protein PIPPin - rat >sp Q63430 Q63430 PIPPIN PROTEIN. Length = 154	gnl PID e1253 426	123	404	86	95	IIOFNV27
164	786932		gi 1050754	2	490	76	87	HUSYH27
165	787078	HER2 receptor [Homo sapiens] >gi 553282 c-erb-2 protein [Homo sapiens] {SUB 737-1031} >gi 553332 HER-2/neu [Homo sapiens] {SUB 1-191} >gi 183989 HER2 receptor (AA at 3) [Homo sapiens] {SUB 740-910} >gi 182169 c-erb B2/neu protein [Homo sapiens] {SUB 1081-}	gi 306840	236	1114	79	79	HCHND12

166	787139			230	625		HBCBA06
167	787283			3	656		HFOYO96
168	788761	MAL3P6.24 [Plasmodium falciparum] >sp O77371 O77371 MAL3P6.24 PROTEIN. Length = 1017	gnl P D e 331 909	2	700	36	HTXFK57
169	788988	(AF023611) Dim1p homolog [Homo sapiens] >sp O14834 O14834 DIM1P HOMOLOG. Length = 142	gi 2565275	70	417	98	HUSGH90
170	789092			2	400		H6EBE80
171	789298	(AF044311) gamma-synuclein [Homo sapiens] >gi 3642775 (AF017256) persyn [Homo sapiens] >gi 3642903 (AF037207) persyn [Homo sapiens] >sp O76070 O76070 PERSYN. Length = 127	gi 3347842	1	489	82	HTSFM20
172	789299			205	381		HBGDD91
173	789718			233	580		IIBGBT30
174	789957	beta-hexosaminidase alpha chain [Homo sapiens] >pir A23561 AOHUBA beta-N- acetylhexosaminidase (EC 3.2.1.52) alpha chain precursor - human >sp P06865 HEXA_HUMAN BETA- HEXOSAMINIDASE ALPHA CHAIN PRECURSOR (EC 3.2.1.52) (N-ACETYL- BETA-GLUCOSAMINIDASE) (BETA-	gi 179458	750	1619	99	HISEM44

175	789977	arginyl-tRNA synthetase, ArgRS [human, ataxia-telangiectasia patients, EBV-lymphoblastoid cells, Peptide, 659 aa] [Homo sapiens] >pir JC4365 JC4365 arginine--tRNA ligase (EC 6.1.1.19) - human Length = 659	bbs 173838	25	2019	94	95	HMEIU30
176	790285	HCG V [Homo sapiens] >sp O60927 O60927 HCG V. Length = 126	gij 3176438	44	391	85	85	HDPCH88
177	790509	human elongation factor-1-delta [Homo sapiens] >pir S34626 S34626 translation elongation factor eEF-1 delta chain - human >sp P29692 EF1D_HUMAN ELONGATION FACTOR 1-DELTA (EF-1-DELTA). Length = 281	gij 38522	227	1108	63	64	HPMGB64
178	790775			950	1351			HJAAO21
179	790888	(AF036956) neuroblastoma apoptosis-related RNA binding protein [Homo sapiens] >sp G4104559 G4104559 NEUROBLASTOMA APOPTOSIS-RELATED RNA BINDING PROTEIN. Length = 490	gij 4104559	2	274	100	100	HE8QE19
180	791506			2	205			HOFMB93
181	791649			3	359			HGBBH10
182	791802			165	695			HWLRH03

39.

183	792002	ADP-ribosylation factor [Homo sapiens] >gi 2088529 ADP-ribosylation factor 5 [Homo sapiens] >gi 438870 ADP- ribosylation factor 5 [Rattus norvegicus] >gnl PID d1014187 ARF5 [Mus musculus] >pir A23741 A23741 ADP-ribosylation factor 5 - human >pir JC4949 JC4	gi 178987	2	635	100	100	HHENT53
184	792291	see GenBank Accession Number U01184 for cDNA; similar to Drosophila melanogaster fil1 in GenBank Accession Number U01182 and Caenorhabditis elegans fil1 homolog in GenBank Accession Number U01183 [Homo sapiens] >sp Q13045 Q13045 FLIGHTLESS-1 PROTEIN HOMOL	gi 2138290	843	3329	96	96	HDPIT69
185	792371			3	665			HUSJW77
186	792660	(AF044773) breakpoint cluster region protein 1 [Homo sapiens] >sp O60558 O60558 BREAKPOINT CLUSTER REGION PROTEIN 1. Length = 138	gi 3002951	116	406	100	100	HCHMC26
187	792782			41	838			HTXJB38
188	792890	(AF001846) lymphoid phosphatase LyP1 [Homo sapiens] >sp G4100632 G4100632 LYMPHOID PHOSPHATASE LYPI. Length = 808	gi 4100632	2	994	90	90	HHESJ29
189	792931			1	576			HEGAW71

190	792943	myosin heavy chain kinase B [Dictyostelium discoideum] >sp P90648 KMHIB_DICDI_MYOSIN HEAVY CHAIN KINASE B (EC 2.7.1.129) (MHCK B). Length = 732	gij 1903458	3	1247	43	68	IIDPRZ79
191	793104			107	250			HKGAJ80
192	793445	desmoyokin - human (fragments) >sp Q09666 AHNK_HUMAN NEUROBLAST DIFFERENTIATION ASSOCIATED PROTEIN AHNAK (DESMOYOKIN) (FRAGMENTS). >gij 17828 AHNAK_nucleoprotein [Homo sapiens] {SUB 1-1683} >gij 897824 AHNAK gene product [Homo sapiens] {SUB 1684-2960} Leng	pir A45259 A 45259	1	723	92	92	HDTEJ86
193	793446			25	255			HIIBGY94
194	793639	(AF044959) NADH:ubiquinone oxidoreductase NDUFS6 subunit [Homo sapiens] >sp O75380 NUMM_HUMAN NADH-UBIQUINONE OXIDOREDUCTASE 13 KD-A SUBUNIT PRECURSOR (EC 1.6.5.3) (EC 1.6.99.3) (COMPLEX I-13KD-A) (CI-13KD-A). Length = 124 100 kDa protein [Rattus norvegicus] >pir S22659 S22659_hypothetical protein, 100K - rat >sp Q62671 100K_RAT 100 KD PROTEIN (EC 6.3.2.-). Length = 889	gij 3348137	1	411	100	100	HLJB172
195	794213		gij 55535	326	691	93	95	HLWCN67
196	795858			1020	1205			HLVDY53



197	795955	c-myc binding protein [Homo sapiens] >sp Q99471 MM1_HUMAN C-MYC BINDING PROTEIN MM-1. >sp D1014706 D1014706 C-MYC BINDING PROTEIN. Length = 167	gn P D d 01 4706	31	507	100	100	100	HUSXX36
198	796359	ribosomal protein L7a large subunit [Homo sapiens] >gi 34203 L7a protein [Homo sapiens] >gi 35512 PLA-X polypeptide [Homo sapiens] >gi 36647 ribosomal protein L7a [Homo sapiens] >gi 56956 ribosomal protein L7a (AA 1-266) [Rattus rattus] >pir S19717 R5HU7A	gi 337495	19	297	100	100	100	HOFNW79
199	796555	DJ366N23.3 (KIAA0173 AND TUBULIN- TYROSINE LIGASE LIKE) (FRAGMENT). Length = 278	sp O75653 O7 5653	1	1086	44	62	44	HLWEW04
200	796675	PEG1/MEST [Homo sapiens] >sp O15007 O15007 PEG1/MEST GENE MRNA. Length = 335	gn P D e 3070 37	44	1027	100	100	100	HSICR25
201	796743	(AF022229) translation initiation factor 6 [Homo sapiens] >gn P D e 304603 b4 integrin interactor [Homo sapiens] >gi 3335506 (AF047433) b(2)gcn homolog [Homo sapiens] >sp P56537 IF6_HUMAN EUKARYOTIC TRANSLATION INITIATION FACTOR 6 (EIF-6) (B4 INTEGRIN INT	gi 2809383	30	842	100	100	100	H6EDU12
202	796792			198	461				HDTII72
203	799668			166	303				HODBC01
204	799669			2	310				HOGAV29

205	799673		2	310		HOFMNS3
206	799674		130	1044		HCHMI60
207	799678	ribosomal protein L18a [Homo sapiens] >gi 3702270 (AC005796) ribosomal protein L18a [Homo sapiens] >gn P D d1029536 (AB007175) ribosomal protein L18a [Homo sapiens] {SUB 111-176} Length = 176	40	345	98	HOFNL25
208	799728		3	179		HBGBG75
209	799748		1	660		IIC11MQ24
210	799760	o361 [Escherichia coli] >gi 1790125 (AE000446) orf, hypothetical protein [Escherichia coli] >pir C65171 C65171 hypothetical 41.0 kD protein in ibpA-gyrB intergenic region - Escherichia coli (strain K-12) Length = 361	1	357	99	I1BGIBF66
211	799805		2	118		HBGDA22
212	800296	CDC37 homolog [Homo sapiens] >gi 1375485 CDC37 homolog [Homo sapiens] >pir G02313 G02313 CDC37 homolog - human >sp Q16543 Q16543 CDC37 HOMOLOG. Length = 378	2	802	89	HDABE68

213	800327	ADP-ribosylation factor-like protein 2 [Homo sapiens] >pir A48259 A48259 ADP- ribosylation factor-like 2 - human >sp P36404 ARL2_HUMAN ADP- RIBOSYLATION FACTOR-LIKE PROTEIN 2. >sp G425655 G425655 ARL2=ADP-RIBOSYLATION FACTOR HOMOLOG. Length = 184	gj 3009501	25	645	99	99	HCHPG41
214	800816			115	351			HODCV09
215	800835	(AF071538) Ets transcription factor PDEF [Homo sapiens] >sp G4007418 G4007418 ETS TRANSCRIPTION FACTOR PDEF. Length = 335	gj 4007418	3	881	96	96	HETJP29
216	805429	RanGAP1 [Homo sapiens] >pir JC5300 JC5300 Ran GTPase activator 1 - human Length = 587	gj 575268	3	683	90	90	HKABS06
217	805458	(AF044221) HCG-1 protein [Homo sapiens] >sp G4105252 G4105252 HCG-1 PROTEIN. Length = 117	gj 4105252	745	1122	100	100	HDQEV55
218	805478			60	644			HDQGR35
219	805805	19 kDa subunit of NADH:ubiquinone oxidoreductase complex (complex I) [Bos taurus] >pir S16208 S16208 NADH dehydrogenase (ubiquinone) (EC 1.6.5.3) 19K chain - bovine >sp P42029 NUPM_BOVIN NADH- UBIQUINONE OXIDOREDUCTASE 19 KD SUBUNIT (EC 1.6.5.3) (EC 1.6.99	gj 599681	2	478	87	90	HOFMH12
220	806486			3	62			HFXJC33

221	806498			518	1741		HIBCA25	
222	806819	acidic ribosomal phosphoprotein (P0) [Homo sapiens] >gi 2935618 (AC004263) 60S ACIDIC RIBOSOMAL PROTEIN; match to P05388 (PID:gi 33041) [Homo sapiens] >pir A27125 R5HUP0 acidic ribosomal protein P0 - human >sp D1026785 D1026785 RIBOSOMAL PROTEIN P0 (FRAGME	gi 190232	3	866	81	84	HOFAC09
223	810870	thrombospondin-4 [Homo sapiens] >pir A55710 TSHUP4 thrombospondin 4 precursor - human Length = 961	gi 311626	2	1333	99	99	HBOEB83
224	811730			2	979			HCHPJ26
225	813025	heat shock protein 86 [Homo sapiens] >sp Q14568 Q14568 HEAT SHOCK PROTEIN 86 (FRAGMENT). Length = 312	gi 292162	106	492	88	89	HOEFD78
226	813233	co-beta glucosidase precursor [Homo sapiens] >gi 337762 prosaposin [Homo sapiens] >gi 337756 sphingolipid activator precursor [Homo sapiens] Length = 524	gi 183231	1	468	81	90	HOEFD17
227	813262			1	345			HFKCA89
228	815637	(AC004003) serine/threonine kinase RICK; match to protein AF027706 (PID:gi 3123887) and mRNA AF027706 (NID:gi 3123886) [Homo sapiens] >gi 3290172 (AF064824) CARD-containing ICE associated kinase [Homo sapiens] >gi 3342910 (AF078530) receptor	gi 3264574	3	461	92	92	HNHDS66

## interacting prote

229	815853	calcyphosine [Homo sapiens] >gi 3075376 (AC004602) CAYP_HUMAN; RD25 [Homo sapiens] >sp Q13938 CAYP_HUMAN CALCYPHOSINE. Length = 189	gnl PID e2458 72	8	667	100	100	HLHAY85
230	815999	S100 calcium-binding protein A13 (S100A13) [Homo sapiens] >pir JC5064 JC5064 S-100 calcium-binding protein A13 - human Length = 98	gnl PID e2682 53	68	421	42	70	HKABX07
231	823427			1	927			HTLGL50
232	823704	(AC004770) BC269730_2 [Homo sapiens] >sp O60427 O60427 BC269730_2. Length = 444	gi 3169158	3	860	67	80	HDABC49
233	824798			307	858			HDQ GK75
234	825018			2	1924			HETIS29
235	825076	Whole ORF continues from bp19 (right after 'tag') to bp1596 ('iga'); similar to chinese hamster phosphatidylserine synthase. [Homo sapiens] Length = 473	gnl PID d100 4031	2	1549	92	92	HE9PJ48

236	825787	EXT2 [Homo sapiens] >gi 1621113 hereditary multiple exostoses gene 2 protein [Homo sapiens] >gi 1519605 multiple exostosis 2 [Homo sapiens] >sp Q93063 EXT2_HUMAN EXOSTOSIN-2 (PUTATIVE TUMOUR SUPPRESSOR PROTEIN EXT2) (MULTIPLE EXOSTOSES PROTEIN 2). Length	gi 1518042	305	2293	100	100	HFONV84
237	826116	BETA CRYSTALLIN S (GAMMA CRYSTALLIN S). >gi 557548 crystallin [Homo sapiens] {SUB 19-106} Length = 177	sp P22914 CR BS_HUMAN	392	682	86	87	HAIJAE27
238	826147	neural specific protein CRMP-2 [Bos taurus] >sp O02675 DPY2_BOVIN DIHYDROPYRIMIDINASE RELATED PROTEIN-2 (DRP-2) (NEURAL SPECIFIC PROTEIN NSP60). Length = 572	gi 1916227	3	503	98	98	HICEPT06
239	827020	(AF027954) Bcl-2-related ovarian killer protein [Rattus norvegicus] >gi 2689660 (AF027707) apoptosis activator Mtd [Mus musculus] >sp O35425 O35425 BCL-2- RELATED OVARIAN KILLER PROTEIN. Length = 213	gi 2645560	12	539	95	97	HHFHE17
240	827586	calmodulin [Plasmodium falciparum] >gi 160128 calmodulin [Plasmodium falciparum] >pir B45594 MCZQF calmodulin - Plasmodium falciparum >sp P24044 CALM_PLAFA CALMODULIN. Length = 149	gi 385234	85	495	49	76	HCHMW40

241	827732	alternate name ygiG; ORF_f123 [Escherichia coli] >gi 1789438 (AE000387) putative kinase [Escherichia coli] >pir H65093 H65093 ygiG protein - Escherichia coli (strain K-12) >sp P31055 FOLB_ECOLI PROBABLE DIHYDRONEOPTERIN ALDOLASE (EC 4.1.2.25) (DHNA). {SUB	gi 882580	181	282	91	95	HBGDE81
242	827735			541	708			HHEDU22
243	827740			716	838			HBNAP17
244	827808			86	1657			HMELR44
245	828251	(AB016869) p70 ribosomal S6 kinase beta [Homo sapiens] >sp D1035383 D1035383 P70 RIBOSOMAL S6 KINASE BETA. Length = 495	gnl P1D d103 5383	134	949	91	91	INGOL64
246	828357			1	768			HKIYP61
247	828449			1	723			HBXCZ22
248	828612	syntaxin 5 [Homo sapiens] >pir G01817 G01817 syntaxin 5 - human Length = 301	gi 886071	68	460	100	100	HNHMY58
249	828647	laminin beta 2 chain [Homo sapiens] >sp P55268 LMB2_HUMAN LAMININ BETA-2 CHAIN PRECURSOR (S- LAMININ). Length = 1798	gnl P1D e2132 86	299	2254	85	85	HRABB47

250	828698	galactokinase [Homo sapiens] >gi 1929895 galactokinase [Homo sapiens] >sp P51570 GALI_HUMAN GALACTOKINASE 1 (EC 2.7.1.6). >gi 3603423 (AF084935) galactokinase [Homo sapiens] {SUB 1-264} Length = 392	gi 1002507	3	1220	83	83	HKG AU37
251	828962	secretory protein [Homo sapiens] >gi 940946 intestinal trefoil factor [Homo sapiens] >pir A48284 A48284 intestinal trefoil factor 3 precursor - human >sp Q07654 ITF_HUMAN INTESTINAL TREFOIL FACTOR PRECURSOR (HPI.B). Length = 80	gi 402483	2	259	78	78	HCHMR52
252	828982	unnamed protein product [unidentified] >gi 189500 p62 [Homo sapiens] >pir A38219 A38219 GAP-associated tyrosine phosphoprotein p62 - human >sp Q07666 Q07666 GAP-ASSOCIATED TYROSINE PHOSPHOPROTEIN P62. >gnl PID e1259626 unnamed protein product [unidentifie	gnl PID e1259 622	1	1176	85	85	HE9PC52
253	829282			289	828			HCHOB95
254	829368			279	512			HWGAA79
255	829751			2	418			HCHMB33
256	829773	(AF109906) G9A [Mus musculus] >sp G3986768 G3986768 G9A. Length = 1000	gi 3986768	26	862	97	98	HMWBV67



257	829934	precursor polypeptide (AA -21 to 782) [Homo sapiens] >pir A35954 A35954 endoplasmin precursor - human >sp P14625 ENPL_HUMAN ENDOPLASMIN PRECURSOR (94 KD GLUCOSE-REGULATED PROTEIN) (GRP94) (GP96 HOMOLOG) (TUMOR REJECTION ANTIGEN 1). Length = 803 dynamitin [Homo sapiens] >sp Q13561 DYNC_HUMAN DYNACTIN, 50 KD ISOFORM (50 KD DYNEIN-ASSOCIATED POLYPEPTIDE) (DYNAMITIN). Length = 406	gi 37261	1142	2356	94	94	HFIIJ68
258	829942		gi 255188	15	1409	85	85	HUFBF69
259	829951			119	262			HIBGBA32
260	830173	death associated protein 5 [Homo sapiens] >sp O60877 O60877 DEATH ASSOCIATED PROTEIN 5. Length = 907	gi PID e1298 888	51	2870	90	90	HETIX39
261	830200			3	638			HBCMF83
262	830365	mevalonate pyrophosphate decarboxylase [Homo sapiens] >sp P53602 ER19_HUMAN DIPHOSPHOMEVALONATE DECARBOXYLASE (EC 4.1.1.33) (MEVALONATE PYROPHOSPHATE DECARBOXYLASE). Length = 400	gi 235682	56	1291	95	95	HUSIG21
263	830456			215	397			HCFBN01

264	830549	guanine nucleotide-binding regulatory protein-beta-2 subunit [Homo sapiens] >gi 339935 transducin beta-2 subunit [Homo sapiens] >gi 3135310 (AF053356) GNB2 [Homo sapiens] >pir B26617 RGHUB2 GTP-binding regulatory protein beta-2 chain - human >sp P11016 GB	gi 386751	1	729	100	100	100	HDPM12
265	830602			24	461				HTLD182
266	830610	zyxin [Homo sapiens] >gnl PID e223417 zyxin [Homo sapiens] >pir G02845 G02845 zyxin - human Length = 572	gnl PID e2182 60	956	1855	94	94	94	HDPRN35
267	830644	(AF104260) hiwi [Homo sapiens] >sp G4038413 G4038413 HIWI (FRAGMENT). Length = 523	gi 4038413	2	391	99	99	99	HTEEU95
268	830707			3	623				HETCJ14
269	830709			2	304				HSSGN20
270	830733			540	725				HSNAD86
271	830768	carboxylesterase hCE-2 [Homo sapiens] >sp Q16859 Q16859 CARBOXYLESTERASE (EC 3.1.1.1) (AL1-ESTERASE) (B-ESTERASE) (MONOBUTYRASE) (COCAINE ESTERASE) (PROCAINE ESTERASE) (METHYLBUTYRASE). Length = 550	gi 1407780	623	2269	99	99	99	HDPMX44
272	830855			1	465				HJPC06

273	830949		2457	2903		HCE5J35
274	830965		139	792		II0IIC/A01
275	830973		354	557		HR0DL42
276	830979	THIOREDOXIN REDUCTASE 2. Length = 526	753	1454	81	HOGCC93
277	830989	La protein [Homo sapiens] >gi 36415 ribonucleoprotein SS-B/La (AA 1-408) [Homo sapiens] >pir A31888/A31888 ribonucleoprotein La - human >sp P05455 LA_HUMAN LUPUS LA PROTEIN (SJOGREN SYNDROME TYPE B ANTIGEN (SS-B)) (LA RIBONUCLEOPROTEIN) (LA AUTOANTIGEN).	3	1382	87	HDQFZ49
278	831134		2	241		HBXEB46
279	831200		3	773		HADXB20
280	831260		892	1095		HLWBR58
281	831531	transcription factor [Homo sapiens] >gi 37058 IIB protein [Homo sapiens] >pir S17654 TWHU2B transcription initiation factor IIB - human >bbs 112738 S300-II, TFIIIB=transcription factor [human, Peptide Partial, 311 aa] [Homo sapiens] {SUB 6-316} Length = 31	93	1172	95	HHPGX85
282	831665		2	1093		HSKDH81

283	831724			1	468				HFEBQ94
284	831884	(AF034800) liprin-alpha3 [Homo sapiens] >sp G3309535 G3309535 LIPRIN- ALPHA3 (FRAGMENT). Length = 443	gi 3309535	20	469	90			HDTGO74
285	831897	laminin B1 [Homo sapiens] >gi 186876 laminin B1 [Homo sapiens] >gi 186913 laminin B1 [Homo sapiens] >pir S13547 MMHUB1 laminin chain B1 precursor - human >sp P07942 LMB1_HUMAN LAMININ BETA-1 CHAIN PRECURSOR (LAMININ B1 CHAIN). Length = 1786	gi 186837	1	1581	92	92		HSKHIV84
286	831922			499	684				HDQIB68
287	831963			188	319				HDPCS84
288	832074	gluconate kinase [Escherichia coli] >gi 1790719 (AE000497) gluconate kinase, thermosensitive glucokinase [Escherichia coli] >pir S56494 S56494 gluconokinase (EC 2.7.1.12) gntV - Escherichia coli >sp P39208 GNTV_ECOLI THERMOSENSITIVE GLUCONOKINASE (EC 2.7.	gi 537110	1	579	42	58		HCRNT71
289	832266			71	433				HNGJU70
290	832309			1891	2226				HBJDT21
291	832342	fatty acid amide hydrolase [Homo sapiens] >sp O00519 O00519 FATTY ACID AMIDE HYDROLASE. Length = 579	gi 2149156	9	224	97	100		HBGDP82

292	832351	unknown product specific to adipose tissue [Homo sapiens] >sp Q15847 Q15847 HYPOTHETICAL 7.9 KD PROTEIN. Length = 76	gnl P1D1d100 8821	47	298	68	68	HFABE30
293	832352	unknown product specific to adipose tissue [Homo sapiens] >sp Q15847 Q15847 HYPOTHETICAL 7.9 KD PROTEIN. Length = 76	gnl P1D1d100 8821	89	277	92	94	HOEKX93
294	832434	Cks1 protein homologue [Homo sapiens] >pir A36670 A36670 protein kinase cdc2 complex subunit CKS1 - human >sp P33551 CKS1_HUMAN CYCLIN- DEPENDENT KINASES REGULATORY SUBUNIT 1 (CKS-1). Length = 79	gil29977	78	335	100	100	HFNAB43
295	832490	growth arrest and DNA-damage-inducible protein [Homo sapiens] >gil403128 [Human gadd45 gene, complete cds.], gene product [Homo sapiens] >pir A39617 A39617 DNA-damage-inducible protein gadd45 - human >sp P24522 GA45_HUMAN GROWTH ARREST AND DNA- DAMAGE-INDU	gil182940	220	798	98	100	HKAKL21
296	832573			30	629			HCHOY13
297	832580	pS2 protein [Homo sapiens] >gil35707 pS2 precursor [Homo sapiens] >gnl P1D1e223341 pS2 [Homo sapiens] >pir A26667 A26667 pS2 protein precursor - human >gil182204 estrogen receptor [Homo sapiens] {SUB 2-84} Length = 84	gil35718	45	362	100	100	H2LAR67

298	833394			274	588				HBGMC47
299	835355	(AF060567) sushi-repeat protein [Homo sapiens] >sp O60687 O60687 SUSHI-REPEAT PROTEIN. Length = 465	gj 3108089	3	1295	99	100		HUSAU05
300	835497	(AJ006064) coronin-like protein [Rattus norvegicus] >sp O89046 O89046 CORONIN-LIKE PROTEIN. Length = 484	gn PID e 331790	334	1584	96	99		HLDDS71
301	835728			2	871				HODAK21
302	835978			643	2019				ITLLEB03
303	836091	PDC-E2 precursor (AA -54 to 561) [Homo sapiens] >pir S01783 XXHIU dihydrolipoamide S-acetyltransferase (EC 2.3.1.12) precursor - human (fragment) >gj 345030 Human 70kd mitochondrial antigen of PBC [unidentified] {SUB 179-500} >sp G254062 G254062 PYRUVATE D	gj 35360	546	2114	99	99		I12CBW86
304	836274	Id4 [Homo sapiens] >gn PID e266418 helix-loop-helix protein [Homo sapiens] >gn PID e1359205 (AL022726) dJ625H18.1 (ID4 Helix-loop-helix DNA binding protein) [Homo sapiens] >gn PID e266418 helix-loop-helix protein [Homo sapiens] >pir G01855 G01855 Id4 -	gj 881546	2	334	98	98		HCLBP52

305	836731	(AF075599) ubiquitin conjugating enzyme 12 [Homo sapiens] >gnl PID d1034111 (AB012191) Nedd8-conjugating enzyme hUbc12 [Homo sapiens] >sp O76069 O76069 UBIQUITIN- CONJUGATING ENZYME E2 (EC 6.3.2.19) (UBIQUITIN-PROTEIN LIGASE) (UBIQUITIN CARRIER PROTEIN). L prolyl 4-hydroxylase alpha (II) subunit [Homo sapiens] >sp O15460 O15460 PROLYL 4-HYDROXYLASE ALPHA (II) SUBUNIT (II). Length = 535	gi 3309661	2	571	100	100	HFXAZ01
306	838014		gi 2439985	3	1574	99	99	HTEHY24
307	838874			271	546			HFPEZ63
308	839120	peptide transporter [Homo sapiens] >pir S13427 A41538 ATP-binding cassette transporter TAP1 - human >gi 34636 ABC- transporter [Homo sapiens] {SUB 61-808} >gi 930122 Y3 gene product [Homo sapiens] {SUB 183-612} Length = 808	gi 36061	100	2169	90	90	HNFY03
309	839611			548	793			HAMF154
310	840138	start position 1 [Homo sapiens] >sp E1335356 E1335356 ASMTL PROTEIN. >gnl PID e1335357 start position 2 [Homo sapiens] {SUB 59-629} Length = 629	gnl PID e1335 356	1	1800	92	93	HFIHW86

311	840616	Homology with Squid retinal-binding protein (PIR Acc. No. A53057) [Caenorhabditis elegans] >sp Q22467 Q22467.T13H5.2 PROTEIN. Length = 1254	gnl PID e1349 397	3	1607	73	86	HMSCY51
312	840780	unknown [Saccharomyces cerevisiae] >pir S58704 S58704 probable membrane protein YIL003w - yeast (Saccharomyces cerevisiae) >gil 558401 incomplete orf, len: 160, CAI: 0.09 similar to MRP_ECOLI P21590 39.9 KD PROTEIN [Saccharomyces cerevisiae] {SUB 1-158} >g	gil 763343	17	880	57	80	H6EDY61
313	840857	(AF071059) zinc finger RNA binding protein [Mus musculus] >sp O88532 O88532.ZINC FINGER RNA BINDING PROTEIN. Length = 1052 cysteine-rich intestinal protein [Homo sapiens] >pir G02666 G02666 cysteine-rich protein 1 - human Length = 77	gil 3293537	459	2669	94	94	HLHDQ83
314	840862		gil 1381638	36	353	100	100	HEPAP58
315	840864			407	1096			HTLHY48
316	840936	homologous to Swiss-Prot accession number P16371 [Homo sapiens] >gil 3850562 (AC005944) GRG_HUMAN; ESPI PROTEIN; AMINO ENHANCER OF SPLIT; AES-1/AES-2; gp130 associated protein GAM [Homo sapiens] >pir G01236 G01236 enhancer of split m9/m10 (groucho protein)	gil 435425	3	668	79	79	HOENU32



317	840938	carbonyl reductase [Sus scrofa] >pir JN0703 JN0703 carbonyl reductase (NADPH) (EC 1.1.1.184) - pig >sp Q29529 CBR2_PIG LUNG CARBONYL REDUCTASE [NADPH] (EC 1.1.1.184) (NADPH-DEPENDENT CARBONYL REDUCTASE) (LCR). Length = 244	gnl PID d100 4479	2	745	65	76	HMCA175
318	841884			677	1324			HLQB145
319	842241	(A J009698) embigin protein [Rattus norvegicus] >sp O88775 O88775 EMBIGIN PROTEIN PRECURSOR. Length = 328	gnl PID e1312 986	2	952	60	75	HOFMD52
320	843712			2	202			HSSGR77
321	844040	ribosomal protein L11 [Caenorhabditis elegans] >pir S27795 S27795 ribosomal protein L11 homolog - Caenorhabditis elegans Length = 195	gij I56201	75	500	42	64	HPTGB84
322	844336	(AB009462) LDL receptor related protein 105 [Homo sapiens] >sp O75074 O75074 LDL RECEPTOR RELATED PROTEIN 105. Length = 770	gnl PID d103 3292	831	2285	68	75	HWMFE21
323	844612	collagen binding protein 2 [Homo sapiens] >pir I52968 I52968 colligin-2 - human >sp P50454 CBP2_HUMAN COLLAGEN- BINDING PROTEIN 2 PRECURSOR (COLLIGIN 2). Length = 418	gnl PID d101 2496	528	1466	96	97	HOFME75
324	844617			556	735			HMVCZ36

325	845251	LIV-1 protein [Homo sapiens] >pir G02273 G02273 LIV-1 protein - human >sp Q13433 Q13433 ESTROGEN REGULATED LIV-1 PROTEIN. Length = 752	gil1256001	23	634	49	67	HBGBB42
326	845764			2	244			HULCF61
327	846187	ATPase alpha subunit (aa 1-1023) [Homo sapiens] >gn P1D1 000505 Na,K-ATPase alpha-subunit [Homo sapiens] >pir A24414 A24414 Na+/K+-exchanging ATPase (EC 3.6.1.37) alpha-1 chain - human >sp P05023 ATN1_HUMAN SODIUM/POTASSIUM- TRANSPORTING ATPASE ALPHA-1 C	gil28927	151	2403	92	92	HDPLV27
328	HBGDH47R			167	241			IIBGDI147
329	HHENQ86R			2	112			HHENQ86
330	HBGBH23R	(AE000161) bacteriophage lambda endopeptidase homolog [Escherichia coli] >pir B64788 B64788 bacteriophage lambda endopeptidase homolog (EC 3.4.-.-) - Escherichia coli (strain K-12) >sp P75719 ENPP_ECOLI PUTATIVE ENDOPEPTIDASE (EC 3.4.-.-). Length = 153	gil1786769	1	213	92	92	HBGBH23
331	HANGA53R	(AF013214) acidic ribosomal phosphoprotein PO [Bos taurus] Length = 302	gil2293577	76	402	80	84	HANGA53

332	HBIMC29R	(AF035959) type-2 phosphatidic acid phosphatase-gamma; phosphatidate phosphohydrolase; phospholipid phosphatase [Homo sapiens] >gi 3025880 (AF056083) phosphatidic acid phosphatase type 2 [Homo sapiens] >gi 2911498 (AF047760) phosphatidic acid phosphohydro (AF061340) F1 ATPase subunit 6 [Artibeus jamaicensis] Length = 226 (AF070447) barrier-to-autointegration factor [Homo sapiens] >sp O75531 O75531 BARRIER-TO-AUTOINTEGRATION FACTOR. Length = 89	gi 3123896	3	317	96	96	HBIMC29
333	HOFAB89R		gi 4164480	86	268	67	82	HOFAB89
334	HAHCP93R		gi 3220255	116	289	69	76	HAHCP93
335	HBGAA76R			14	232			HBGAA76
336	HGBGT12R	A (DNA packaging;641) [Bacteriophage lambda] >pir D04333 JVPAL DNA- packaging protein A - phage lambda Length = 641	gi 215106	2	349	95	95	HGBGT12
337	HGBBH53R	Actin [Drosophila melanogaster] >pir S14851 S14851 actin - fruit fly (Drosophila melanogaster) . >sp Q24228 Q24228 ACTIN. Length = 100	gi 7550	2	445	93	97	HGBBH53

338	HTXPI29R	aldolase A (EC 4.1.3.13) [Homo sapiens] >gil28597 aldolase A (AA 1-364) [Homo sapiens] >pir S14084 ADHUA fructose-bisphosphate aldolase (EC 4.1.2.13) A - human >sp P04075 ALFA_HUMAN FRUCTOSE-BISPHOSPHATE ALDOLASE A (EC 4.1.2.13) (MUSCLE-TYPE ALDOLASE). {S}	gil178351	1	453	86	86	HTXPI29
339	HOFMG33R	ATPase [Equus caballus] >sp P48662 ATP6_HORSE ATP SYNTHASE A CHAIN (EC 3.6.1.34) (PROTEIN 6). Length = 226	gil577577	28	309	57	62	HOFMG33
340	HCGAC11R			1	345			HCGAC11
341	HCIAC54R			37	168			HCIAC54
342	HBGAA54R			1	282			HBGAA54
343	HAOMC34R	calpactin I heavy chain (p36) [Bos taurus] >pir A03081 LUBO36 annexin II - bovine >sp P04272 ANX2_BOVIN ANNEXIN II (LIPOCORTIN II) (CALPACTIN I HEAVY CHAIN) (CHROMOBINDIN 8) (P36) (PROTEIN I) (PLACENTAL ANTICOAGULANT PROTEIN IV) (PAP-IV). {SUB 2-339} Leng	gil162779	2	115	73	80	HAOMC34
344	H2LAU88R	copine I [Homo sapiens] >sp Q99829 Q99829 COPINE I. Length = 537	gil1791257	1	576	95	95	H2LAU88
345	HDPJR77R	DNA topoisomerase II [Homo sapiens] >gil38325 DNA topoisomerase II [Homo sapiens] {SUB 448-681} Length = 1031	gil288565	3	311	100	100	HDPJR77

346	HTTIO41R	docking protein [Homo sapiens] >pir A29440 A29440 signal recognition particle receptor - human Length = 638	gi 30866	90	404	94	95	HTTIO41
347	H2CBU29R	electron transport flavoprotein [Homo sapiens] >pir A31998 A31998 electron transfer flavoprotein alpha chain precursor - human >sp P13804 ETFA_HUMAN ELECTRON TRANSFER FLAVOPROTEIN ALPHA-SUBUNIT PRECURSOR (ALPHA-ETF) >gnl PID e1331769 (AJ224002) electron	gi 182251	2	442	100	100	H2CBU29
348	HBMVA11R	GARS protein [Homo sapiens] >sp Q15374 Q15374 GARS PROTEIN. Length = 433	gnl PID d100 7383	1	108	81	84	HBMVA11
349	HDPUL86R	GC kinase [Homo sapiens] >pir A53714 A53714 protein kinase (EC 2.7.1.37) BL44 - human >sp Q12851 Q12851 GC KINASE. Length = 819	gi 531820	3	317	64	65	HDPUL86
350	HTXNT16R	GTP-binding protein [Homo sapiens] >gi 577779 GTP-binding protein [Homo sapiens] >pir A55014 A55014 GTP-binding protein - human >sp P55039 DRG2_HUMAN DEVELOPMENTALLY REGULATED GTP-BINDING PROTEIN DRG2. Length = 364	gi 577779	2	463	100	100	HTXNT16
351	HBGAA13R	H (tail component;853) [Bacteriophage lambda] >pir G43008 TLBPHL minor tail protein precursor H - phage lambda Length = 853	gi 215120	1	267	97	97	HBGAA13

352	HLXNA54R	heat shock protein HSP27 [Homo sapiens] >gi 433598 28 kDa heat shock protein [Homo sapiens] >gi 1913885 heat shock protein [Homo sapiens] >pir S12102 HHHU27 heat shock protein 27 - human >sp G248440 G248440 28 KDA HEAT SHOCK PROTEIN HOMOLOG FRAGMENT 2. {S	gi 32478	2	256	98	98	HLXNA54
353	HCHOH37R	Hep27 protein [Homo sapiens] >pir S66665 S66665 nuclear protein Hep27 - human >sp Q13268 HE27_HUMAN HEP27 PROTEIN (PROTEIN D). {SUB 24-280} Length = 280	gi 1079566	337	564	75	81	HCHOH37
354	H2LAX93R	histone H2B [Gallus gallus] >gi 63434 histone H2B [Gallus gallus] >gi 63452 histone H2B (AA 1 - 126) [Gallus gallus] >gi 63456 histone H2B (AA 1 - 126) [Gallus gallus] >gi 63458 histone H2B [Gallus gallus] >gi 63460 histone H2B (AA 1 - 126) [Gallus gallus] homologue to elongation factor 1-gamma from A.salina [Homo sapiens] >gi 31104 elongation factor-1-gamma [Homo sapiens] >pir S22655 S22655 translation elongation factor eEF-1 gamma chain - human >sp P26641 EF1G_HUMAN ELONGATION FACTOR 1-GAMMA (EF- 1-GAMMA).	gi 211845	191	505	89	96	H2LAX93
355	HWAFFW10R		gi 31102	3	434	98	98	HWAFFW10

356	HBNAB19R	human complement C1r [Homo sapiens] >pir A24170 C1HURB complement subcomponent C1r (EC 3.4.21.41) precursor - human >sp P00736 C1R_HUMAN COMPLEMENT C1R COMPONENT PRECURSOR (EC 3.4.21.41). Length = 705	gij 179644	2	193	98	98	HBNAB19
357	HBGDD17R	hypothetical protein [Escherichia coli] >gij 1786774 (AE000161)orf, hypothetical protein [Escherichia coli] >pir G64788 G64788 hypothetical protein b0561 - Escherichia coli (strain K-12) Length = 247	gij 1778474	1	207	98	98	HBGDD17
358	HBIAB72R	hypoxanthine phosphoribosyltransferase [Sus scrofa] >sp P79306 P79306 HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE (FRAGMENT). Length = 85	gnl PID e2919 69	2	169	81	86	HBIAB72
359	HFIEH41R	interferon-gamma induced protein [Homo sapiens] >pir I54501 I54501 interferon gamma-induced protein IFI 16 - human >sp Q16666 IFI16_HUMAN GAMMA- INTERFERON-INDUCIBLE PROTEIN IFI-16 (INTERFERON-INDUCIBLE MYELOID DIFFERENTIATION TRANSSCRIPTIONAL ACTIVATOR). Le	gij 184569	5	406	96	97	HFIEH41
360	H2CBB43R	J (tail:host specificity;1132) [Bacteriophage lambda] >pir D43009 QSBPL host specificity protein J - phage lambda Length = 1132	gij 215125	2	400	99	99	H2CBB43

361	H2CBQ77R	J (tail:host specificity; 1132) [Bacteriophage lambda] >pir D43009 QSBPL host specificity protein J - phage lambda Length = 1132	3	272	97	97	H2CBQ77
362	HATAO24R	J (tail:host specificity; 1132) [Bacteriophage lambda] >pir D43009 QSBPL host specificity protein J - phage lambda Length = 1132	2	247	71	71	HATAO24
363	HOEMK06R	K (tail component; 199) [Bacteriophage lambda] >pir H43009 TJBPKL tail assembly protein K - phage lambda Length = 199	3	149	97	97	HOEMK06
364	HADCH03R	mitochondrial acetoacetyl-CoA thiolase precursor [Homo sapiens] Length = 427	2	256	83	83	HADCH03
365	HCHAG30R	Mta1 [Rattus norvegicus] >pir A54766 A54766 metastasis-associated protein mta-1 - rat >sp Q62599 MTA1_RAT METASTASIS-ASSOCIATED PROTEIN MTA1. Length = 703	2	271	92	92	HCHAG30
366	HOFAD96R	NADH dehydrogenase subunit 4L [Felis catus] >sp P48931 NULM_FELCA NADH-UBIQUINONE OXIDOREDUCTASE CHAIN 4L (EC 1.6.5.3). Length = 98	2	253	50	52	HOFAD96
367	H2CBX07R	Nin 221 (pept unknown; 221) [Bacteriophage lambda] >pir G43011 Q1BP1L multiple specificity phosphoprotein phosphatase (EC 3.1.3.-) - phage lambda >sp P03772 PP_LAMBD SERINE/THREONINE PROTEIN PHOSPHATASE (EC 3.1.3.16). Length = 221	2	184	100	100	H2CBX07



368	HDPLN02R	nuclear corepressor KAP-1 [Homo sapiens] Length = 835	gi 1699027	149	454	90	90	HDPLN02
369	HT4FU27R	nuclear corepressor KAP-1 [Homo sapiens] Length = 835	gi 1699027	96	287	95	95	HT4FU27
370	HAEAI26R	open reading frame A; putative [Homo sapiens] Length = 84	gi 190369	109	291	78	80	HAEAI26
371	HCDAR56R	p23 [Homo sapiens] >pir A56211 A56211 progesterone receptor-related protein p23 - human >sp Q15185 Q15185 (P23). Length = 160	gi 438652	2	208	90	92	HCDAR56
372	HCDCW35R	precursor [Homo sapiens] Length = 631	gi 36049	3	155	78	84	HCDCW35
373	H2CBN76R	proteasome subunit C5 [Homo sapiens] >gnl PID e 1334433 (AL031259) C5 (proteasome subunit HC5) [Homo sapiens] >pir S15973 SNHUC5 multicatalytic endopeptidase complex (EC 3.4.99.46) chain C5 - human >sp P20618 PRC5_HUMAN PROTEASOME COMPONENT C5 (EC 3.4.99.4	gnl PID d 100 1116	3	464	99	99	H2CBN76
374	HAGFX49R	proteasome subunit C5 [Homo sapiens] >gnl PID e 1334433 (AL031259) C5 (proteasome subunit HC5) [Homo sapiens] >pir S15973 SNHUC5 multicatalytic endopeptidase complex (EC 3.4.99.46) chain C5 - human >sp P20618 PRC5_HUMAN PROTEASOME COMPONENT C5 (EC 3.4.99.4	gnl PID d 100 1116	1	288	98	100	HAGFX49

375	HNEEG64R	put. major coat protein (AA 1-341) [Bacteriophage phi-80] >pir S03314 VHBP80 major capsid protein - phage phi-80 >sp P05481 HEAD_BPPH8 MAJOR HEAD PROTEIN (GPE)(GP5) (MAJOR COAT PROTEIN). Length = 341	gil 5769	17	232	81	97	HNEEG64
376	HTXKR32R	putative nucleotide-binding protein [Homo sapiens] >pir JC4010 JC4010 nucleotide-binding protein - human >sp P53384 NBP_HUMAN NUCLEOTIDE-BINDING PROTEIN (NBP). Length = 320	gil 5644	3	374	100	100	HTXKR32
377	HAIBZ58R	putative start codon [Homo sapiens] Length = 210	gil 895845	2	433	65	65	HAIBZ58
378	H6EAF46R	rexa (exclusion;279) [Bacteriophage lambda] >gil 5068 reading frame (rex1 protein) [Bacteriophage 434] >pir E43010 IMBPAL rexA protein - phage lambda Length = 279	gil 215146	43	333	92	93	H6EAF46
379	H2LA W60R	ribosomal protein L27a [Homo sapiens] >pir S55914 S55914 ribosomal protein L27a - human Length = 148	gil 550017	3	545	88	88	H2LA W60
380	H2LAK40R	ribosomal protein L31 [Sus scrofa] >gil 36130 ribosomal protein L31 (AA 1-125) [Homo sapiens] >gil 57115 ribosomal protein L31 (AA 1-125) [Rattus norvegicus] >pir S05576 R5HU31 ribosomal protein L31 - human >pir A26417 R5RT31 ribosomal protein L31 - rat >gn	gnl PID e2764 36	76	483	77	80	H2LAK40

381	H2LAY71R	ribosomal protein L35 [Homo sapiens] >pir G01477 G01477 ribosomal protein L35 - human Length = 123	gil562074	70	495	100	100	H2LAY71
382	HCHAH62R	ribosomal protein L8 [Homo sapiens] >gil57704 ribosomal protein L8 [Rattus rattus] >gil1527178 ribosomal protein L8 [Mus musculus] >pir J0177 R5RTL8 ribosomal protein L8, cytosolic - rat >pir JN0923 JN0923 ribosomal protein L8, cytosolic - human >gil3851	gil433899	1	222	76	76	HCHAH62
383	H6EEF31R	ribosomal protein S2 [Rattus norvegicus] >sp O55211 O55211 RIBOSOMAL PROTEIN S2. Length = 257	gil2920825	1	300	89	91	H6EEF31
384	HDPBT55R	RNAse L inhibitor [Mus musculus] >sp O88793 O88793 RNAse L INHIBITOR. Length = 599	gil3273417	71	127	81	86	HDPBT55
385	HASAW80R	S.macroura Wilms tumour protein [Sminthopsis macroura] Length = 239	gil987118	1	162	90	98	HASAW80
386	HCHAF25R	SSR alpha subunit [Homo sapiens] >pir J38246 J38246 SSR alpha subunit - human Length = 286	gil551638	2	421	95	95	HCHAF25
387	HLTHH84R	UMP synthase [Homo sapiens] >pir A30148 A30148 UMP synthase - human Length = 480	gil340168	2	391	99	99	HLTHH84
388	H2CBU20R			39-	143			H2CBU20
389	HADAA62R			3	218			HADAA62
390	HADDC09R			16	174			HADDC09
391	HAIAB75R			2	211			HAIAB75

392	HAMGA37R	3	119	HAMGA37
393	HAQA110R	1	81	HAQA110
394	HBFMEE95R	3	218	HBFMEE95
395	HBGBH24R	1	81	HBGBH24
396	HBGBT78R	1	69	HBGBT78
397	HBGCB06R	3	140	HBGCB06
398	HBGDO01R	1	156	HBGDO01
399	HBIBJ73R	3	341	HBIBJ73
400	HBJLE85R	3	398	HBJLE85
401	HBNAD53R	2	187	HBNAD53
402	HBNAT63R	54	173	HBNAT63
403	HCE4H65R	2	193	HCE4H65
404	HCFLJ44R	92	274	HCFLJ44
405	HCHMW05R	3	221	HCHMW05
406	HCHNR50R	2	103	HCHNR50
407	HE8DS01R	2	64	HE8DS01
408	HFEBP31R	109	276	HFEBP31

409	HLDXE36R	6	167	HLDXE36
410	HLTGV28R	181	414	HLTGV28
411	HODFW25R	42	308	HODFW25
412	HOEMQ91R	1	129	HOEMQ91
413	HOGBG56R	57	386	HOGBG56
414	HOSMT44R	2	151	HOSMT44
415	HRAEE04R	51	191	HRAEE04
416	HULFN65R	3	272	HULFN65
417	HWLVW23R	1	153	HWLVW23
418	HWLWE77R	149	289	HWLWE77

The first column of Table 1 shows the "SEQ ID NO:" for each of the 418 breast/ovarian cancer antigen polynucleotide sequences of the invention.

The second column in Table 1, provides a unique "Sequence/Contig ID" identification for each breast, ovarian, breast cancer and/or ovarian cancer associated sequence. The third column in Table 1, "Gene Name," provides a putative identification of the gene based on the sequence similarity of its translation product to an amino acid sequence found in a publicly accessible gene database, such as GenBank (NCBI). The great majority of the cDNA sequences reported in Table 1 are unrelated to any sequences previously described in the literature. The fourth column, in Table 1, "Overlap," provides the database accession no. for the database sequence having similarity. The fifth and sixth columns in Table 1 provide the location (nucleotide position nos. within the contig), "Start" and "End", in the polynucleotide sequence "SEQ ID NO:X" that delineate the preferred ORF shown in the sequence listing as SEQ ID NO:Y. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the portion of SEQ ID NO:X delineated by the nucleotide position nos. "Start" and "End". Also provided are polynucleotides encoding such proteins and the complementary strand thereto. The seventh and eighth columns provide the "% Identity" (percent identity) and "% Similarity" (percent similarity) observed between the aligned sequence segments of the translation product of SEQ ID NO:X and the database sequence.

The ninth column of Table 1 provides a unique "Clone ID" for a clone related to each contig sequence. This clone ID references the cDNA clone which contains at least the 5' most sequence of the assembled contig and at least a portion of SEQ ID NO:X was determined by directly sequencing the referenced clone. The reference clone may have more sequence than described in the sequence listing or the clone may have less. In the vast majority of cases, however, the clone is believed to encode a full-length polypeptide. In the case where a clone is not full-length, a full-length cDNA can be obtained by methods described elsewhere herein.

Table 3 indicates public ESTs, of which at least one, two, three, four, five, ten, or more of any one or more of these public ESTs are optionally excluded from the invention.

SEQ ID NO:X (where X may be any of the polynucleotide sequences disclosed in the sequence listing as SEQ ID NO:1 through SEQ ID NO:418) and the translated SEQ ID NO:Y (where Y may be any of the polypeptide sequences disclosed in the sequence listing as SEQ

ID NO:418 through SEQ ID NO:836) are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X has uses including, but not limited to, in designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the related cDNA clone  
5 contained in a library deposited with the ATCC. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y have uses that include, but are not limited to, generating antibodies which  
10 bind specifically to the breast/ovarian cancer antigen polypeptides, or fragments thereof, and/or to the breast/ovarian cancer antigen polypeptides encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions  
15 of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over  
20 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing the related cDNA clone  
25 (deposited with the ATCC, as set forth in Table 1). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO:X.

The predicted amino acid sequence can then be verified from such deposits.  
30 Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to vectors or plasmids which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC on:

5    **Table 2**

ATCC Deposits	Deposit Date	ATCC Designation Number
LP01, LP02, LP03, LP04, LP05, LP06, LP07, LP08, LP09, LP10, LP11,	May-20-97	209059, 209060, 209061, 209062, 209063, 209064, 209065, 209066, 209067, 209068, 209069
LP12	Jan-12-98	209579
LP13	Jan-12-98	209578
LP14	Jul-16-98	203067
LP15	Jul-16-98	203068
LP16	Feb-1-99	203609
LP17	Feb-1-99	203610
LP20	Nov-17-98	203485
LP21	Jun-18-99	PTA-252
LP22	Jun-18-99	PTA-253
LP23	Dec-22-99	PTA-1081

each is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as shown in Table 5. These deposits are referred to as  
10    “the deposits” herein. The tissues from which the clones were derived are listed in Table 5, and the vector in which the cDNA is contained is also indicated in Table 5. The deposited material includes the cDNA clones which were partially sequenced and are related to the SEQ ID NO:X described in Table 1 (column 9). Thus, a clone which is isolatable from the ATCC Deposits by use of a sequence listed as SEQ ID NO:X may include the entire coding  
15    region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene. Although the sequence listing lists only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to complete the sequence of the DNA included in a clone isolatable from the



ATCC Deposits by use of a sequence (or portion thereof) listed in Table 1 by procedures hereinafter further described, and others apparent to those skilled in the art.

Also provided in Table 5 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res.* 16:7583-7600 (1988); Altling-Mees, M. A. and Short, J. M., *Nucleic Acids Res.* 17:9494 (1989)) and pBK (Altling-Mees, M. A. et al., *Strategies* 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into *E. coli* strain XL-1 Blue, also available from Stratagene.

Vectors pSport1, pCMVSPORT 1.0, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus* 15:59 (1993). Vector lacmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR<sup>®</sup>2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: (1991).

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the cDNA contained in a deposited cDNA clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include, but are not limited to, preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the cDNA contained in the related cDNA clone in the deposit, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or the related cDNA clone (See, e.g., columns 1 and 9 of Table 1). The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in a deposited library. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by the the dDNA in the related cDNA clone contained in a deposited library, are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the complement of the coding strand of the related cDNA clone contained in a deposited library.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence would unduly burden the disclosure of this application. Accordingly, for each "Contig Id" listed in the first column of Table 3, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described in the second column of Table 3 by the general formula of a-b, each of which are uniquely defined for the SEQ ID NO:X corresponding to that Contig Id in Table 1. Additionally, specific embodiments are directed to polynucleotide sequences excluding at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. for each Contig Id which may be

included in column 3 of Table 3. In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example.

Table 3

Sequence/ Contig ID	General formula	Genbank Accession No.
419266	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1899 of SEQ ID NO:1, b is an integer of 15 to 1913, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:1, and where b is greater than or equal to a + 14.	T68585, T68665, T86313, T86314, R12356, R31374, R32873, R37282, R84617, R85369, R99171, H48474, N23871, N58201, N74557, W90334, AA031318, AA031427, AA130231, AA256587
429114	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1411 of SEQ ID NO:2, b is an integer of 15 to 1425, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:2, and where b is greater than or equal to a + 14.	R20542, R42676, R42676, R20542, R61501, H08662, H77556, H97365, N24198, N33135, N74546, N93573, W02941, W52194, AA004624, AA004721, AA046710, AA235395, AA235479
506777	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 340 of SEQ ID NO:3, b is an integer of 15 to 354, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:3, and where b is greater than or equal to a + 14.	
508678	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 500 of SEQ ID NO:4, b is an integer of 15 to 514, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:4, and where b is greater than or equal to a + 14.	W37175, AA121532, AA127694
508968	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	T71941, T94428, T94514, H02313, N26913, N47870, N66244, N92418, W31301, W42459, W42564, AA084031, AA126786, AA258050, AA459772

	formula of a-b, where a is any integer between 1 to 2021 of SEQ ID NO:5, b is an integer of 15 to 2035, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:5, and where b is greater than or equal to a + 14.	
509029	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1182 of SEQ ID NO:6, b is an integer of 15 to 1196, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:6, and where b is greater than or equal to a + 14.	R11213, R11271, H14072, H14071, H51531, H66637, H66636, W23707, W35307, AA025586, AA025710, AA058796, AA113917
519726	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 610 of SEQ ID NO:7, b is an integer of 15 to 624, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:7, and where b is greater than or equal to a + 14.	AA236015, AA236085, AA256106
522632	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 287 of SEQ ID NO:8, b is an integer of 15 to 301, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:8, and where b is greater than or equal to a + 14.	
524655	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 672 of SEQ ID NO:9, b is an integer of 15 to 686, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:9, and where b is greater than or equal to a + 14.	T66495, R15869, R39696, H16266, H20784, H22599, N68150, W58001, W57856
525847	Preferably excluded from the present	

	invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 383 of SEQ ID NO:10, b is an integer of 15 to 397, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:10, and where b is greater than or equal to a + 14.	
530306	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 549 of SEQ ID NO:11, b is an integer of 15 to 563, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:11, and where b is greater than or equal to a + 14.	
532818	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 429 of SEQ ID NO:12, b is an integer of 15 to 443, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:12, and where b is greater than or equal to a + 14.	AA188990, AA191040
533385	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2424 of SEQ ID NO:13, b is an integer of 15 to 2438, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:13, and where b is greater than or equal to a + 14.	
533532	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2333 of SEQ ID NO:14, b is an integer of 15 to 2347, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID	T94240, T77619, R13236, R17515, R33142, R33294, R39249, R40318, R42609, R42609, R40318, R75952, H03594, H12337, H12391, H70913, H70916, H70996, H71001, H87858, H70913, N21374, N31326, N35068, N35435, N43807, N45045, W46431, W46486, W51917, AA019546, AA018858, AA056764, AA056767, AA058441, AA058445, AA083228, AA083269, AA115939, AA122236, AA147307, AA159802,

	NO:14. and where b is greater than or equal to a + 14.	AA165015. AA165642. AA181869, AA186834, AA252269. AA255892. AA463239, AA463240
534852	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1992 of SEQ ID NO:15, b is an integer of 15 to 2006, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:15. and where b is greater than or equal to a + 14.	T55469, T63434. R10603. R10604, H50597, H92640, H94634. W39162, W93243, W94634, W94719, N90240. AA053667, AA167312, AA253414. AA253389
537910	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 972 of SEQ ID NO:16, b is an integer of 15 to 986, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:16, and where b is greater than or equal to a + 14.	R23785
538460	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1575 of SEQ ID NO:17, b is an integer of 15 to 1589, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:17, and where b is greater than or equal to a + 14.	R13084. R40514, R40514, R55303, R55402, W67446
539577	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 832 of SEQ ID NO:18, b is an integer of 15 to 846, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:18, and where b is greater than or equal to a + 14.	T49208, N35488, AA088419, AA127572, AA127649, AA156316, AA169250
548379	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2178 of SEQ ID NO:19, b	R23778, H70824

	is an integer of 15 to 2192, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:19, and where b is greater than or equal to a + 14.	
548489	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 997 of SEQ ID NO:20, b is an integer of 15 to 1011, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:20, and where b is greater than or equal to a + 14.	T49861, T49862, T56225, T56367, T72170, T72948, T92867, T74728, R08625, R08719, R17408, R24674, R25174, R25378, R25997, R26800, R28401, R31330, R31589, R42642, R45259, R42642, R45259, R62552, R62553, R66386, R67726, R68781, R68878, H25120, H25121, H41115, H41190, H41191, R84227, R87629, H53386, H64419, H64476, H72640, H72641, H64419, H99301, N22341, N25846, N29370, N29843, N47918, N57261, N59763, N63813, N94171, W23786, W45524, W72111, W77797, AA010718, AA011164, AA033553, AA033554, AA062727, AA062741, AA062784, AA069811, AA075470, AA075471, AA081844, AA083492, AA084442, AA100358, AA126263, AA126354, AA136544, AA136648, AA146862, AA146863, AA179509, AA179540, AA179775, AA180492, AA181719, AA188903, AA189140, AA226959, AA227247
548595	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2005 of SEQ ID NO:21, b is an integer of 15 to 2019, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:21, and where b is greater than or equal to a + 14.	T61537, T69836, R10679, R42501, R46798, R42501, R46798, H05289, H05822, H12239, H16816, H40312, R86905, R86985, N21432, N73268, W73102, N91565, AA033533, AA053026, AA121547, AA127684, AA190356, AA195451, AA226965, AA232522, AA258142
549337	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2008 of SEQ ID NO:22, b is an integer of 15 to 2022, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:22, and where b is greater than or equal to a + 14.	
549777	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1112 of SEQ ID NO:23, b	T81557, R27931, R38730, R39493, R39494, R66845, R67942, R69099, R69214, R69613, R69703, R69740, R72430, R72478, R73090, R73091, R73872, R73955, R82662, R82715, H01096, H01097, H72113, N76139, W58493, W72884, W74409, W94644, W92532,



	is an integer of 15 to 1126, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:23, and where b is greater than or equal to a + 14.	AA022916, AA022917, AA039661, AA039660, AA043439, AA054965, AA152376, AA148360, AA181225, AA188435
553091	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2584 of SEQ ID NO:24, b is an integer of 15 to 2598, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:24, and where b is greater than or equal to a + 14.	
553827	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 397 of SEQ ID NO:25, b is an integer of 15 to 411, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:25, and where b is greater than or equal to a + 14.	
556350	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 643 of SEQ ID NO:26, b is an integer of 15 to 657, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:26, and where b is greater than or equal to a + 14.	T70920, R01856, R37402, H21077, H21531, R94734, N29364, N32255, N80553, W07675, W58340, W58661, W67208, W67352, AA039658, AA039659, AA046392, AA055650, AA058365, AA070442, AA088882, AA102056, AA134144, AA165363, AA171617, AA173761, AA173771, AA252260, AA464575, AA464679
556351	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1889 of SEQ ID NO:27, b is an integer of 15 to 1903, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:27, and where b is greater than or equal to a + 14.	T70981, R01855, R13494, H21076, H24431, H24460, R94817, N47912, AA040086, AA040133, AA055706, AA056162, AA058484, AA102055, AA102304, AA130304, AA173608, AA195879
557007	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	H13846, H13894, H16354, H20742, H20743, R97935, R97936, H87445, N29633, AA015991, AA045671, AA045670, AA099154, AA099252

	sequence described by the general formula of a-b, where a is any integer between 1 to 1319 of SEQ ID NO:28, b is an integer of 15 to 1333, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:28, and where b is greater than or equal to a + 14.	
558140	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1313 of SEQ ID NO:29, b is an integer of 15 to 1327, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:29, and where b is greater than or equal to a + 14.	T62991, W58535, W58500, AA053629, AA083878, AA112892, AA157250, AA157345, AA194089, AA253436, AA250750
558456	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 695 of SEQ ID NO:30, b is an integer of 15 to 709, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:30, and where b is greater than or equal to a + 14.	
558708	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1094 of SEQ ID NO:31, b is an integer of 15 to 1108, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:31, and where b is greater than or equal to a + 14.	R38385, W24640, W48793, W49619
574789	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 512 of SEQ ID NO:32, b is an integer of 15 to 526, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:32, and where b is greater than or equal to a + 14.	N49156

578203	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 541 of SEQ ID NO:33, b is an integer of 15 to 555, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:33, and where b is greater than or equal to a + 14.	AA149853
585385	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 333 of SEQ ID NO:34, b is an integer of 15 to 347, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:34, and where b is greater than or equal to a + 14.	
588869	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 736 of SEQ ID NO:35, b is an integer of 15 to 750, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:35, and where b is greater than or equal to a + 14.	
597076	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1277 of SEQ ID NO:36, b is an integer of 15 to 1291, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:36, and where b is greater than or equal to a + 14.	
598656	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1521 of SEQ ID NO:37, b is an integer of 15 to 1535, where both a and b correspond to the positions of	

	nucleotide residues shown in SEQ ID NO:37, and where b is greater than or equal to a + 14.	
611880	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 281 of SEQ ID NO:38, b is an integer of 15 to 295, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:38, and where b is greater than or equal to a + 14.	
614329	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1286 of SEQ ID NO:39, b is an integer of 15 to 1300, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:39, and where b is greater than or equal to a + 14.	T49777, T51334, T49778, T66835, T66836, T78401, R33579, R33684, R34361, R34476, R72556, R75702, H01591, H02719, H13232, H13599, H13942, H13943, H63376, H80729, H80730, H89353, H89539, H99395, N26995, N32930, N40116, N42081, N50408, N50460, N63978, N67308, N92847, W46413, AA126994, AA128141, AA146958, AA146957, AA425764
616066	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 201 of SEQ ID NO:40, b is an integer of 15 to 215, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:40, and where b is greater than or equal to a + 14.	
620956	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 460 of SEQ ID NO:41, b is an integer of 15 to 474, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:41, and where b is greater than or equal to a + 14.	
621889	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	

	between 1 to 411 of SEQ ID NO:42, b is an integer of 15 to 425, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:42, and where b is greater than or equal to a + 14.	
624017	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1173 of SEQ ID NO:43, b is an integer of 15 to 1187, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:43, and where b is greater than or equal to a + 14.	T61010, AA071044, AA088260, AA098798, AA102017, AA100707, AA111883, AA113305, AA121495, AA133235, AA131438, AA132011, AA132866, AA143457, AA146581, AA146805, AA146928, AA155613, AA155609, AA158090, AA158263, AA164694, AA165591, AA176429, AA226820
651784	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 501 of SEQ ID NO:44, b is an integer of 15 to 515, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:44, and where b is greater than or equal to a + 14.	W32583, W68240, W94174, AA251670, AA252011, AA252266, AA425209
651826	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1485 of SEQ ID NO:45, b is an integer of 15 to 1499, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:45, and where b is greater than or equal to a + 14.	T47384, T47385, T60137, T60194, T71947, T95050, T95146, R25340, R25476, R26117, R26301, R27566, R27664, R28180, R33393, R35872, R35873, R36483, R48329, R48438, R62139, R62244, R66007, R66008, R66764, R70718, R70719, R73674, R73761, R74132, R76569, R76643, R77265, R77312, R78827, R79686, R79687, R81316, R81751, H00804, H00891, H01415, H01416, H02522, H03673, H13925, H13926, H24743, H26369, H26727, H26728, H27132, H27480, H27663, H28192, H28235, H41929, H41977, H42604, H43209, H43258, H45278, H45348, H53585, H53906, H61785, H61786, H78337, H78338, H87337, H87871, H95183, N27090, N27092, N40499, N40502, N99158, W24165, W60193, AA039817, AA041344, AA074512, AA079058, AA079156, AA079157, AA085829, AA085974, AA100095, AA113304, AA142843, AA149898, AA156331, AA157820, AA157895, AA158552, AA159177, AA176093, AA179607, AA179608, AA176333, AA187637, AA186769, AA188622, AA188742, AA188975
653282	Preferably excluded from the present	

	invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 379 of SEQ ID NO:46, b is an integer of 15 to 393, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:46, and where b is greater than or equal to a + 14.	
657122	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 224 of SEQ ID NO:47, b is an integer of 15 to 238, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:47, and where b is greater than or equal to a + 14.	
661442	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 925 of SEQ ID NO:48, b is an integer of 15 to 939, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:48, and where b is greater than or equal to a + 14.	R18101, AA424721
664914	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1757 of SEQ ID NO:49, b is an integer of 15 to 1771, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:49, and where b is greater than or equal to a + 14.	T86944, T87027, R11421, T81153, T81380, R17243, R17453, R19171, R27826, R27927, R35295, R35940, R41854, R42800, R48191, R48192, R49457, R51209, R52247, R53413, R41854, R42800, R49457, R55257, R55475, R59472, R71390, R81811, R81915, H05137, H07974, H30702, H42552, H57923, H58015, N71127, N74282, N75329, N93224, W01557, W04382, W04780, W23438, W35253, W38865, AA176204, AA194869, AA199875, AA251414
666654	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 383 of SEQ ID NO:50, b is an integer of 15 to 397, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID	

	NO:50, and where b is greater than or equal to a + 14.	
667084	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1621 of SEQ ID NO:51, b is an integer of 15 to 1635, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:51, and where b is greater than or equal to a + 14.	R71869, R71870, H22387, H27160, H46592, H61204, H62108, N25274, N94410, AA026642, AA069188, AA069189, AA076423, AA076388, AA076533, AA076540, AA122346, AA121039, AA121092, AA133121, AA143471, AA143470, AA143728, AA156363, AA156404, AA158498, AA159190, AA159201, AA159286, AA160335, AA159837, AA159573, AA160367, AA159548, AA160456, AA160697, AA160789, AA179329, AA181540, AA182669, AA186881, AA186887, AA188535, AA188540, AA190669, AA190973, AA191557, AA235457, AA458511, AA418203
667380	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1766 of SEQ ID NO:52, b is an integer of 15 to 1780, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:52, and where b is greater than or equal to a + 14.	T87574, R10276, R10277, T79847, R49790, R49832, R59538, R59539, R86940, R87067, R87722, R98577, R98578, R99022, R99795, H72692, H93036, H93942, H93941, N54059, N62326, N64719, N66726, N73888, N74171, N91734, N93505, W02054, W03949, W04337, W21317, AA192562, AA192563, AA223984, AA224049
669530	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 476 of SEQ ID NO:53, b is an integer of 15 to 490, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:53, and where b is greater than or equal to a + 14.	T49160, T49161, H41659, R88196, W60799, W60930, AA046915, AA046972, AA069703, AA464334
671315	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1930 of SEQ ID NO:54, b is an integer of 15 to 1944, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:54, and where b is greater than or equal to a + 14.	
671993	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	

	between 1 to 980 of SEQ ID NO:55, b is an integer of 15 to 994, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:55, and where b is greater than or equal to a + 14.	
674618	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 314 of SEQ ID NO:56, b is an integer of 15 to 328, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:56, and where b is greater than or equal to a + 14.	
675027	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1475 of SEQ ID NO:57, b is an integer of 15 to 1489, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:57, and where b is greater than or equal to a + 14.	T86474, AA133454, AA203346
677202	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1269 of SEQ ID NO:58, b is an integer of 15 to 1283, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:58, and where b is greater than or equal to a + 14.	T47486, T47487, T47666, T50413, T50493, T50519, T51852, T53234, T57067, T60776, T40856, T93579, T94432, T94435, T96391, R43542, R43542, H21618, H73240, H88867, H88868, H89122, H88868, H89122, N21997, N22243, N22815, N45720, N48998, N52063, N59239, N62103, N66419, N66708, N66782, N67139, N67283, N67447, N68047, N70159, N71198, N74676, N76707, N78333, N80016, N92971, N93518, W05738, W45694, W48845, W80602, AA057801, AA063330, AA064827, AA065165, AA065178, AA065179, AA069552, AA070491, AA070949, AA070969, AA071333, AA071358, AA074331, AA081280, AA111928, AA112051, AA132018, AA132121, AA147357, AA157065, AA157085, AA157890, AA160054, AA181729, AA182765, AA187698, AA186444, AA196168, AA196244, AA224187
678504	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 726 of SEQ ID NO:59, b is	



	an integer of 15 to 740, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:59, and where b is greater than or equal to a + 14.	
678985	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1277 of SEQ ID NO:60, b is an integer of 15 to 1291, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:60, and where b is greater than or equal to a + 14.	
682161	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 957 of SEQ ID NO:61, b is an integer of 15 to 971, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:61, and where b is greater than or equal to a + 14.	
683476	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 604 of SEQ ID NO:62, b is an integer of 15 to 618, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:62, and where b is greater than or equal to a + 14.	
691146	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1124 of SEQ ID NO:63, b is an integer of 15 to 1138, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:63, and where b is greater than or equal to a + 14.	T48865, T48866, T48901, T47562, T48902, T54258, T54365, T69783, T70768, R08012, R09058, R09059, T83437, T84082, T99021, R09059, R19174, R21551, R22562, R28286, R48757, R48758, R49683, R49683, R62406, R62407, R70222, R75607, R77000, R78400, R78401, R80802, H02840, H03734, H24549, H26291, H26447, H27912, H43630, H47817, R83903, R83904, R94147, H49533, H49773, H50716, H50820, H87446, H87553, H93471, H93472, H98814, N22867, N32137, N32762, N34334, N35009, N36932, N43763, N46205, N52251, N56805, N72290, N95794, W02713, W02886, W17176, W24905, W25571, W25688,

		W67795, W72687, W72962, W77793, W79704, W81376, W86301, W86316, AA025519, AA025959, AA026653, AA029556, AA029704, AA079472, AA121306, AA136679, AA148681, AA148680, AA181745, AA425923
693589	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 404 of SEQ ID NO:64, b is an integer of 15 to 418, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:64, and where b is greater than or equal to a + 14.	
694991	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2822 of SEQ ID NO:65, b is an integer of 15 to 2836, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:65, and where b is greater than or equal to a + 14.	
698303	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2291 of SEQ ID NO:66, b is an integer of 15 to 2305, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:66, and where b is greater than or equal to a + 14.	T83582, T84417, T85606, R66380, R67111, R76298, H96019, H96020, N25659, N25661, N34260, N34263, N70618, W05500, W15421, W23670, W39659, AA015855, AA033569, AA033570, AA044566, AA044583, AA178933, AA179025
698669	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1893 of SEQ ID NO:67, b is an integer of 15 to 1907, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:67, and where b is greater than or equal to a + 14.	T47115, T47116, R48786, R48893, R55495, R71847, R78934, R79033, R82776, H26587, H27077, R97760, H59232, H79115, H79116, N22948, N23658, N26858, N28757, N39967, N71599, W24648, W60157, W67490, W67491, W67815, W72921, W94215, AA009634, AA026899, AA026900, AA029244, AA029040, AA031846, AA031847, AA032073, AA034285, AA034992, AA036865, AA037006, AA040908, AA039990, AA040521, AA040522, AA040773, AA043726, AA044071, AA044182, AA042948, AA043067, AA046606, AA046721, AA062914, AA074334, AA076039, AA076203, AA079763, AA079764, AA082550, AA085926, AA099318,

		AA099836, AA102385, AA101039, AA101040, AA112571, AA112572, AA114828, AA114951, AA128001, AA128082, AA126986, AA128134, AA128459, AA129910, AA131403, AA131503, AA147437, AA147438, AA150961, AA151051, AA156785, AA156855, AA157912, AA157913, AA158544, AA158545, AA158554, AA158553, AA211822, AA460840, AA461144
705696	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 801 of SEQ ID NO:68, b is an integer of 15 to 815, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:68, and where b is greater than or equal to a + 14.	H20141, H20156, H20236, H20250, H49965, H50007, H50487, W92252, AA045116, AA134141, AA142968
706393	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1136 of SEQ ID NO:69, b is an integer of 15 to 1150, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:69, and where b is greater than or equal to a + 14.	T48975, T51242, T51357, T59673, T59807, T62725, T62875, T72330, T97577, R01168, R21893, R22365, R35745, R41863, R41863, R63676, R65881, R72862, R73334, R75659, R75767, H02871, H03430, H03512, H14924, H23660, H30020, H30277, H39675, H40069, H40278, H40526, H41667, H41700, H43170, H43670, H45130, H45172, H45173, H45433, H46542, H46952, H46953, H62390, H78695, H78777, H84781, H85405, H92309, N20534, N33402, N38945, N57790, N57945, N59752, W94488, W94489, AA044423, AA043057, AA081370, AA081371, AA099447, AA112623, AA112622, AA143199, AA143214, AA149467, AA149553, AA157049, AA157201, AA157952, AA157953, AA158049, AA158435, AA158837, AA158841, AA161074, AA161078, AA180395, AA251447, AA419021, AA428783, AA429093
707357	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 330 of SEQ ID NO:70, b is an integer of 15 to 344, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:70, and where b is greater than or equal to a + 14.	
707360	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	

	formula of a-b, where a is any integer between 1 to 434 of SEQ ID NO:71, b is an integer of 15 to 448, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:71, and where b is greater than or equal to a + 14.	
707375	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2811 of SEQ ID NO:72, b is an integer of 15 to 2825, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:72, and where b is greater than or equal to a + 14.	T54138, T65139, T65330, T80324, T83140, R00512, R00612, R19513, R31469, R31470, R47795, R77921, R78022, R80012, H02327, H02429, H06404, H06405, H08607, H08608, H14264, H18370, H19266, H19267, H21399, H21471, H47094, H47185, R85467, R87496, R87501, R87581, R88189, R88226, R88227, N23376, N32357, N58463, N66212, N93661, N99103, W19083, W24383, W68601, W68602, W68723, W68745, AA016149, AA040296, AA056973, AA135439, AA135519, AA135580, AA135856, AA158858, AA161122, AA226730, AA226764, AA227471, AA227481, AA232259
707754	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 496 of SEQ ID NO:73, b is an integer of 15 to 510, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:73, and where b is greater than or equal to a + 14.	
711172	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 444 of SEQ ID NO:74, b is an integer of 15 to 458, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:74, and where b is greater than or equal to a + 14.	
712248	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 363 of SEQ ID NO:75, b is an integer of 15 to 377, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:75, and where b is greater than or	

	equal to $a + 14$ .	
715445	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 2056 of SEQ ID NO:76, $b$ is an integer of 15 to 2070, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:76, and where $b$ is greater than or equal to $a + 14$ .	T88778, T97557, T97604, R17189, R27615, R30849, R41740, R48616, R41740, H12351, R93768, R98882, R98972, H59983, N23156, N32736, N34539, N55086, N62785, N67224, N77297, N78823, N79734, W07252, W90651, AA037793, AA037794, AA055196, AA055286, AA113425, AA233917, AA234165, AA258602, AA258548, AA426581, AA429080
716362	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 983 of SEQ ID NO:77, $b$ is an integer of 15 to 997, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:77, and where $b$ is greater than or equal to $a + 14$ .	
716835	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 1319 of SEQ ID NO:78, $b$ is an integer of 15 to 1333, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:78, and where $b$ is greater than or equal to $a + 14$ .	
716947	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 546 of SEQ ID NO:79, $b$ is an integer of 15 to 560, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:79, and where $b$ is greater than or equal to $a + 14$ .	
717685	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 3189 of SEQ ID NO:80, $b$ is an integer of 15 to 3203, where both $a$	T54040, N35800, W45088, AA122232, AA121109, AA126030, AA126152, AA155618, AA155656

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:80, and where b is greater than or equal to $a + 14$ .	
719755	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1696 of SEQ ID NO:81, b is an integer of 15 to 1710, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:81, and where b is greater than or equal to $a + 14$ .	
720389	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1365 of SEQ ID NO:82, b is an integer of 15 to 1379, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:82, and where b is greater than or equal to $a + 14$ .	
720903	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 664 of SEQ ID NO:83, b is an integer of 15 to 678, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:83, and where b is greater than or equal to $a + 14$ .	
721348	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2789 of SEQ ID NO:84, b is an integer of 15 to 2803, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:84, and where b is greater than or equal to $a + 14$ .	
721562	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	

	formula of a-b, where a is any integer between 1 to 1264 of SEQ ID NO:85, b is an integer of 15 to 1278, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:85, and where b is greater than or equal to a + 14.	
722775	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2571 of SEQ ID NO:86, b is an integer of 15 to 2585, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:86, and where b is greater than or equal to a + 14.	
724463	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 371 of SEQ ID NO:87, b is an integer of 15 to 385, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:87, and where b is greater than or equal to a + 14.	
727501	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2486 of SEQ ID NO:88, b is an integer of 15 to 2500, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:88, and where b is greater than or equal to a + 14.	
728418	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1395 of SEQ ID NO:89, b is an integer of 15 to 1409, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.	
728920	Preferably excluded from the present	

	invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1322 of SEQ ID NO:90, b is an integer of 15 to 1336, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.	
732958	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 773 of SEQ ID NO:91, b is an integer of 15 to 787, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:91, and where b is greater than or equal to a + 14.	
733134	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1643 of SEQ ID NO:92, b is an integer of 15 to 1657, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.	T49547, T49558, T49559, T49560, T49561, T49649, T49650, T70062, T70129, T75532, T95137, R17573, T27052, R19790, R42912, R52618, R53272, R42912, R59922, R59923, R65930, H08841, H08925, H47546, H47547, H47774, H47784, H48119, H64949, H64950, H69959, H69960, H80517, H80569, H81281, H81337, H87618, H87619, H88959, H89042, H95657, H95712, H95729, H88959, H98860, N20108, N23582, N27446, N34733, N49675, N51841, N75517, N78965, N93975, W05310, W17334, W40344, W52084, W52929, W72818, W72819, W86046, W92307, W92294, AA009783, AA009892, AA022930, AA022980, AA024699, AA024734, AA037408, AA045887, AA045888, AA062821, AA081026, AA082088, AA082420, AA102801, AA199861, AA199931, AA220961, AA223217, AA223456, AA224153, AA224177, AA224137, AA224138, AA224341, AA232349, AA232533, AA232117, AA458900, AA459095, AA463299
734099	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 471 of SEQ ID NO:93, b is an integer of 15 to 485, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:93, and where b is greater than or	R22895, H87448



	equal to $a + 14$ .	
734599	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 750 of SEQ ID NO:94, b is an integer of 15 to 764, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:94, and where b is greater than or equal to $a + 14$ .	
736019	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 693 of SEQ ID NO:95, b is an integer of 15 to 707, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:95, and where b is greater than or equal to $a + 14$ .	T41219, T50359, T56829, T58426, T58458, T60928, T60984, T64158, T64287, R27157, H03484, H03579, H22546, H22547, H28310, H44067, H44146, R83796, H48481, H48645, H57243, H66162, H66163, H82370, N21110, N21188, N27461, N29155, N29743, N31124, N32398, N39884, N56818, N57165, N57228, N57403, N68904, N73978, N77833, N93027, N93818, N67112, W00894, W00923, W02234, W16676, W21379, W44969, AA064843, AA070697, AA070876, AA071332, AA071265, AA076379, AA076308, AA079524, AA079572, AA081231, AA081401, AA083774, AA083775, AA130308, AA130309, AA132056, AA132160, AA143132, AA146882, AA146883, AA165057, AA164722, AA166939, AA181133, AA187371, AA187804, AA188118, AA186447, AA186448, AA187105, AA187150, AA188273
738268	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 801 of SEQ ID NO:96, b is an integer of 15 to 815, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:96, and where b is greater than or equal to $a + 14$ .	T48287, T48288, T54477, T54511, R34064, R36907, R49496, R49496, R75625, R75724, H12225, H16384, H19466, H19543, H42166, H42988, H54780, H99297, N22733, N26471, N74933, N93468, W15461, W47542, W47590, N90997, AA010700, AA010701, AA056728, AA088699, AA126219, AA132934, AA156291, AA165516, AA165558, AA176293, AA173448, AA189056, AA233515, AA459831, AA460011
738911	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 644 of SEQ ID NO:97, b is an integer of 15 to 658, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:97, and where b is greater than or equal to $a + 14$ .	H22593, H52836

739226	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 235 of SEQ ID NO:98, b is an integer of 15 to 249, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:98, and where b is greater than or equal to a + 14.	T57824, N63155, AA027845
739527	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 738 of SEQ ID NO:99, b is an integer of 15 to 752, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:99, and where b is greater than or equal to a + 14.	
740710	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3045 of SEQ ID NO:100, b is an integer of 15 to 3059, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:100, and where b is greater than or equal to a + 14.	
742980	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1668 of SEQ ID NO:101, b is an integer of 15 to 1682, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:101, and where b is greater than or equal to a + 14.	T71993, R12901, R40053, H14591, H14696, R83485, H50584, H50585, H89958, H89966, H89973, H89980, N26005, N34777, N36638, N36637, N44503, N67682, N76121, N79613, W03491, W05571, W31276, W49653, W49727, AA009708, AA009798, AA035612, AA042894, AA043030, AA062953, AA115370, AA133278, AA181268, AA181269, AA193206
744331	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 924 of SEQ ID NO:102, b is an integer of 15 to 938, where both a and b correspond to the positions of	R25354, R49789, R71735, R71740, H73502, H79224, H87423, H99515, H99516, N24751, N32707, N44511, N52325, N67764, N75095, N93879, W40372, W69127, W69094, W74698, W74736, AA026984, AA035176, AA149088, AA262739, AA464357, AA430724

	nucleotide residues shown in SEQ ID NO:102, and where b is greater than or equal to a + 14.	
744751	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1998 of SEQ ID NO:103, b is an integer of 15 to 2012, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:103, and where b is greater than or equal to a + 14.	
745750	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1080 of SEQ ID NO:104, b is an integer of 15 to 1094, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:104, and where b is greater than or equal to a + 14.	
746285	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2283 of SEQ ID NO:105, b is an integer of 15 to 2297, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:105, and where b is greater than or equal to a + 14.	T87719, T87928, R99975, R99976, H64714, H65205, H92423, H65205, N47296, N48612, N58085, N58926, N64294, N64508, N72401, N80294, N93405, W04791, W21447, W94582, W95317, AA024856, AA024939, AA037672, AA037673, AA070416, AA075508, AA075507, AA101263, AA148029, AA147953, AA169726, AA171461, AA173095, AA464821
746416	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 428 of SEQ ID NO:106, b is an integer of 15 to 442, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:106, and where b is greater than or equal to a + 14.	
747851	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	N44767, W44754

	between 1 to 1005 of SEQ ID NO:107, b is an integer of 15 to 1019, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:107, and where b is greater than or equal to a + 14.	
750632	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 697 of SEQ ID NO:108, b is an integer of 15 to 711, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:108, and where b is greater than or equal to a + 14.	H48882, W23677, W35110, AA133857
751315	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 729 of SEQ ID NO:109, b is an integer of 15 to 743, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:109, and where b is greater than or equal to a + 14.	
754009	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 781 of SEQ ID NO:110, b is an integer of 15 to 795, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:110, and where b is greater than or equal to a + 14.	
754634	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1318 of SEQ ID NO:111, b is an integer of 15 to 1332, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:111, and where b is greater than or equal to a + 14.	N21429
756637	Preferably excluded from the present invention are one or more	N44651, W76461

	polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 729 of SEQ ID NO:112, b is an integer of 15 to 743, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:112, and where b is greater than or equal to a + 14.	
756833	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1676 of SEQ ID NO:113, b is an integer of 15 to 1690, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:113, and where b is greater than or equal to a + 14.	
756878	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 606 of SEQ ID NO:114, b is an integer of 15 to 620, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:114, and where b is greater than or equal to a + 14.	R12122
757332	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 528 of SEQ ID NO:115, b is an integer of 15 to 542, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:115, and where b is greater than or equal to a + 14.	
760835	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 511 of SEQ ID NO:116, b is an integer of 15 to 525, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:116, and where b is greater than or	

	equal to $a + 14$ .	
761760	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 714 of SEQ ID NO:117, b is an integer of 15 to 728, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:117, and where b is greater than or equal to $a + 14$ .	
762520	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 934 of SEQ ID NO:118, b is an integer of 15 to 948, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:118, and where b is greater than or equal to $a + 14$ .	T86617, T86618, R47814, R49961, R71921, R71968, H28225, H28275, R94939, R95025, R97173, R97174, R99726, R99904, H52435, H52436, H58879, H58880, H66345, H66395, H80709, H80710, W87663, W87664, AA046620, AA046867, AA055456, AA102380, AA121314, AA150579, AA197300
764461	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 197 of SEQ ID NO:119, b is an integer of 15 to 211, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:119, and where b is greater than or equal to $a + 14$ .	
764517	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1294 of SEQ ID NO:120, b is an integer of 15 to 1308, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:120, and where b is greater than or equal to $a + 14$ .	
765132	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2502 of SEQ ID NO:121, b is an integer of 15 to 2516, where both	

	a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:121, and where b is greater than or equal to a + 14.	
765667	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1125 of SEQ ID NO:122, b is an integer of 15 to 1139, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:122, and where b is greater than or equal to a + 14.	T81691, N27595
767113	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2100 of SEQ ID NO:123, b is an integer of 15 to 2114, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:123, and where b is greater than or equal to a + 14.	
767204	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 569 of SEQ ID NO:124, b is an integer of 15 to 583, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:124, and where b is greater than or equal to a + 14.	
767400	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1973 of SEQ ID NO:125, b is an integer of 15 to 1987, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:125, and where b is greater than or equal to a + 14.	
767962	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	T59753, R21255, R21256, R23274, R23364, R71913, R71956, H12633, H12686, H99087, N26954, N33518, N43798, N62998, N66835, N71124, N71156, N74144, N79907, W01554,

	formula of a-b, where a is any integer between 1 to 1437 of SEQ ID NO:126, b is an integer of 15 to 1451, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:126, and where b is greater than or equal to a + 14.	W05537, W19994, W44368, W46357, W46193, W47163, W47284, W52537, W55854, W80804, W80878, W92021, W92022, N90420, AA002178, AA022578, AA022579, AA029899, AA029987, AA034181, AA036856, AA036913, AA043237, AA043566, AA071518, AA082340, AA122159, AA120962, AA146944, AA147449, AA148081, AA151266, AA151267, AA156459
768040	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1220 of SEQ ID NO:127, b is an integer of 15 to 1234, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:127, and where b is greater than or equal to a + 14.	
769956	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 849 of SEQ ID NO:128, b is an integer of 15 to 863, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:128, and where b is greater than or equal to a + 14.	R68817, R68925, R75906, H14626, H82146, H93109, H93237, N32098, N35721, N45410, N75570, W03043, W04850, AA029607, AA262861, AA463956, AA464092
770133	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1224 of SEQ ID NO:129, b is an integer of 15 to 1238, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:129, and where b is greater than or equal to a + 14.	
770289	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 365 of SEQ ID NO:130, b is an integer of 15 to 379, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:130, and where b is greater than or equal to a + 14.	



771964	<p>Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1772 of SEQ ID NO:131, b is an integer of 15 to 1786, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:131, and where b is greater than or equal to a + 14.</p>	<p>T53984, T55243, T51230, T77632, T91326, T80819, T81219, T84909, T95454, T97320, T99226, T99269, R16575, R16634, R19765, R22987, R23096, R33095, R33188, R37437, R39255, R45185, R45185, R62594, R62642, H03891, H03892, H08679, H08680, H20556, H20650, H46154, H46155, R88298, R90733, R90759, R92224, R92332, R97325, H57663, H58503, H61709, H61913, H62747, H66685, H68924, H68954, H80053, H83342, H95786, H96135, N20464, N20472, N24026, N25491, N35235, N35419, N38769, N44900, N48399, N53146, N55089, N55095, N57767, N58580, N59732, N63942, N70290, N71759, N74938, N77300, N98411, W23555, W52690, W52160, W56557, W56635, W56598, W56594, W73408, W74230, W79843, W93916, AA031492, AA070868, AA071019, AA088788, AA100685, AA112926, AA176829, AA176851, AA193034, AA194065, AA194180, AA194579, AA194703, AA195416, AA195532, AA233792, AA233783, AA233900, AA233920, AA234128, AA234169, AA252704, AA252831, AA416743, AA418391, AA418440</p>
772582	<p>Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 960 of SEQ ID NO:132, b is an integer of 15 to 974, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:132, and where b is greater than or equal to a + 14.</p>	
773387	<p>Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 620 of SEQ ID NO:133, b is an integer of 15 to 634, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:133, and where b is greater than or equal to a + 14.</p>	
773827	<p>Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1841 of SEQ ID NO:134,</p>	

	b is an integer of 15 to 1855, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:134, and where b is greater than or equal to a + 14.	
774108	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 903 of SEQ ID NO:135, b is an integer of 15 to 917, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:135, and where b is greater than or equal to a + 14.	T96288, R31388, R32886, R63543, R63597, R75811, R75812, H20285, H20509, H20599, H21238, H24872, H29854, H29945, H41103, H41208, H44188, H44189, R85628, R91367, H83459, H83571, H97165, H97164, N25639, N29652, N29777, N32407, N32413, N32580, N32835, N41918, N42281, N56607, N57152, N57196, N69818, N70613, N93340, N93928, N94454, W24358, W25163, W30800, W37904, W37964, W40428, W68631, W68632, W70339, W80994, W81096, W81716, W81253, W81543, W81544, W94206, AA004372, AA011346, AA016002, AA028888, AA029626, AA029627, AA044028, AA044350, AA062804, AA081035, AA131270, AA131354, AA131371
774636	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1257 of SEQ ID NO:136, b is an integer of 15 to 1271, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:136, and where b is greater than or equal to a + 14.	T54747, T69827, R14146, R50592, R55502, R73615, R73937, H41540, R84981, R85103, R87495, R88553, R88554, R88556, R88818, R88839, R89675, R91235, H51003, H51004, H51581, H79057, N70799, W02680, AA232327, AA232417, AA464467
775339	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2003 of SEQ ID NO:137, b is an integer of 15 to 2017, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:137, and where b is greater than or equal to a + 14.	
775582	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 923 of SEQ ID NO:138, b is an integer of 15 to 937, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:138, and where b is greater than or	T62486, T62631, H14642, R85991, H73603, N54912, N68727, N80228, N91617, W38518, W67302, W67418, AA171395, AA214500, AA215291, AA464035

	equal to $a + 14$ .	
775779	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 2745 of SEQ ID NO:139, $b$ is an integer of 15 to 2759, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:139, and where $b$ is greater than or equal to $a + 14$ .	
777809	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 1227 of SEQ ID NO:140, $b$ is an integer of 15 to 1241, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:140, and where $b$ is greater than or equal to $a + 14$ .	
778927	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 3391 of SEQ ID NO:141, $b$ is an integer of 15 to 3405, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:141, and where $b$ is greater than or equal to $a + 14$ .	T50777, T50939, R11800, R19713, R31403, R32898, R44269, R44269, R55431, R60041, R60103, R69554, R74340, R74434, H20427, H26615, H26660, H42495, H43482, R85644, H51488, H68618, N58157, N58231, N77611, W39692, W45048, W56828, W57633, AA052900, AA057808, AA074705, AA122120, AA121079, AA121231, AA259051, AA464470
779262	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 2254 of SEQ ID NO:142, $b$ is an integer of 15 to 2268, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:142, and where $b$ is greater than or equal to $a + 14$ .	R11844, R71241, R71292, H00159, H88551, H90726, H98059, N28770, N58442, N78033, W32671, AA035075, AA112651, AA112652, AA130035, AA215309, AA251209
779392	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 1743 of SEQ ID NO:143, $b$ is an integer of 15 to 1757, where both	R25284, R36255, R36256, R42970, R46635, R42970, R46635, H28773, N52867, N70541, N77890, W05403, W05783, AA085067, AA085066, AA204650, AA210753, AA211713, AA251462, AA252456, AA460350, AA460780

	a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:143, and where b is greater than or equal to a + 14.	
780149	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1048 of SEQ ID NO:144, b is an integer of 15 to 1062, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:144, and where b is greater than or equal to a + 14.	
780583	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1016 of SEQ ID NO:145, b is an integer of 15 to 1030, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:145, and where b is greater than or equal to a + 14.	
780960	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 800 of SEQ ID NO:146, b is an integer of 15 to 814, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:146, and where b is greater than or equal to a + 14.	
781469	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2664 of SEQ ID NO:147, b is an integer of 15 to 2678, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:147, and where b is greater than or equal to a + 14.	T95791, H18820, H19074, H22604, H40723, H45802, H46056, H47074, H47156, H86819, H86886, H88675, H88724, H88972, H89058, H88972, N28987, N36053, N39668, N47281, W19145, W68543, W68544, N91577, AA044679, AA044896, AA430011
781556	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	T94861, T94906, R21516, R26869, R27098, R36258, R37965, R37966, R78172, H03413, H04116, H14531, H45546, R96826, R98130, N51409, N52365, N64272, N74939, N75136,

	formula of a-b, where a is any integer between 1 to 1014 of SEQ ID NO:148, b is an integer of 15 to 1028, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:148, and where b is greater than or equal to a + 14.	W23556, W35208, AA187823, AA191525, AA429367
781771	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1411 of SEQ ID NO:149, b is an integer of 15 to 1425, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:149, and where b is greater than or equal to a + 14.	T95420, T99529, R50341, R52125, R72608, R72630, R72677, R72701, H26733, H26734, H30106, H59788, H82441, N75150, W42750, W42840
782033	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 766 of SEQ ID NO:150, b is an integer of 15 to 780, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:150, and where b is greater than or equal to a + 14.	H53100, H53207, H97410, H98035, N30753, N68541, W42491, W42641, W57808, AA046603, AA046753, AA136886, AA136997, AA143419, AA143420
782105	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1052 of SEQ ID NO:151, b is an integer of 15 to 1066, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:151, and where b is greater than or equal to a + 14.	R97486, H72940, W90139
782122	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1635 of SEQ ID NO:152, b is an integer of 15 to 1649, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:152, and where b is greater than or equal to a + 14.	T54379, T60348, T61029, T54271, T57801, R10793, T78907, T78959, R49078, R55635, R67844, R67845, R69587, R72600, R72666, H04742, H04830, H16978, H24654, H26129, H26308, H26395, H26467, H28100, H28205, H28252, H28895, H28896, H30485, H39554, H42595, H42603, H42662, H43740, H44345, H44346, H44546, H44547, H44960, H45012, H45860, R88120, R88214, H51204, H58080, H58081, H64553, H64654, H70033, H70034, H86451, H70034, H99833, N24525, N29867, N30752, N35500, N39259, N42463, N44804,

		N52550, N53985, N57289, N58726, N63349, N67624, N67663, N68157, N70299, N80615, N93230, N94595, N98489, W19633, W23803, W25087, W31034, W37981, W37982, W42579, W44389, W49677, W57614, W57871, W58142, W67781, W67840, W68147, W68474, W68699, W68791, W69717, W80749, W80837, N89879, AA025233, AA025568, AA025686, AA026020, AA033846, AA039625, AA039693, AA046842, AA047013, AA057608, AA057676, AA064637, AA064680, AA074448, AA083591, AA098837, AA102142, AA113374, AA113402, AA115525, AA114948, AA128972, AA128973, AA133142, AA146949, AA148086, AA149283, AA149377, AA160012, AA160688, AA172144, AA180932, AA182561
783135	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 646 of SEQ ID NO:153, b is an integer of 15 to 660, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:153, and where b is greater than or equal to a + 14.	
783245	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 591 of SEQ ID NO:154, b is an integer of 15 to 605, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:154, and where b is greater than or equal to a + 14.	
783247	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 681 of SEQ ID NO:155, b is an integer of 15 to 695, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:155, and where b is greater than or equal to a + 14.	AA155638
783413	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	H58751, H93683, H93684, N93167, W19186, W19958, W38771, N91367

	sequence described by the general formula of a-b, where a is any integer between 1 to 766 of SEQ ID NO:156, b is an integer of 15 to 780, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:156, and where b is greater than or equal to a + 14.	
784407	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1113 of SEQ ID NO:157, b is an integer of 15 to 1127, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14.	
784548	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1268 of SEQ ID NO:158, b is an integer of 15 to 1282, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14.	
785075	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1491 of SEQ ID NO:159, b is an integer of 15 to 1505, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14.	
785677	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 722 of SEQ ID NO:160, b is an integer of 15 to 736, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:160, and where b is greater than or equal to a + 14.	

786238	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 981 of SEQ ID NO:161, b is an integer of 15 to 995, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:161, and where b is greater than or equal to a + 14.	
786389	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1111 of SEQ ID NO:162, b is an integer of 15 to 1125, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:162, and where b is greater than or equal to a + 14.	
786929	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 409 of SEQ ID NO:163, b is an integer of 15 to 423, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:163, and where b is greater than or equal to a + 14.	
786932	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1628 of SEQ ID NO:164, b is an integer of 15 to 1642, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:164, and where b is greater than or equal to a + 14.	
787078	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1101 of SEQ ID NO:165, b is an integer of 15 to 1115, where both a and b correspond to the positions of	



	nucleotide residues shown in SEQ ID NO:165, and where b is greater than or equal to a + 14.	
787139	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1052 of SEQ ID NO:166, b is an integer of 15 to 1066, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:166, and where b is greater than or equal to a + 14.	
787283	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 643 of SEQ ID NO:167, b is an integer of 15 to 657, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:167, and where b is greater than or equal to a + 14.	R22724
788761	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1012 of SEQ ID NO:168, b is an integer of 15 to 1026, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:168, and where b is greater than or equal to a + 14.	
788988	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 760 of SEQ ID NO:169, b is an integer of 15 to 774, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:169, and where b is greater than or equal to a + 14.	
789092	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	AA234588

	between 1 to 388 of SEQ ID NO:170, b is an integer of 15 to 402, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:170, and where b is greater than or equal to a + 14.	
789298	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 782 of SEQ ID NO:171, b is an integer of 15 to 796, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:171, and where b is greater than or equal to a + 14.	
789299	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 464 of SEQ ID NO:172, b is an integer of 15 to 478, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:172, and where b is greater than or equal to a + 14.	
789718	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 642 of SEQ ID NO:173, b is an integer of 15 to 656, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:173, and where b is greater than or equal to a + 14.	
789957	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1877 of SEQ ID NO:174, b is an integer of 15 to 1891, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:174, and where b is greater than or equal to a + 14.	T51260, T61941, T62167, T77034, T90753, R38108, N32708, N92379, W24621, W42543, W42478, AA128007, AA128031, AA134234, AA424998
789977	Preferably excluded from the present invention are one or more	T56442, T78292, R37940, R56008, R56009, R56573, R56574, H11080, N34431, N48665,

	polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2147 of SEQ ID NO:175, b is an integer of 15 to 2161, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:175, and where b is greater than or equal to a + 14.	AA010749, AA011177, AA070806, AA070882, AA146859, AA147636, AA147691, AA164223, AA164224, AA210729, AA210859, AA243063, AA243070, AA464493, AA464494
790285	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2397 of SEQ ID NO:176, b is an integer of 15 to 2411, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:176, and where b is greater than or equal to a + 14.	T66279, T66328, T84164, T85098, R24232, R24233, H03657, H03658, H98526, H98556, H99618, N22728, N29400, N32172, N33953, N41460, N69471, N70552, N73722, W03893, W44579, W72407, W76486, W78102, W79410, N90963, AA044816, AA044841, AA086039, AA086121, AA088877, AA102298, AA130887, AA131529, AA131603, AA181784, AA182515, AA190450, AA191392, AA223757
790509	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1324 of SEQ ID NO:177, b is an integer of 15 to 1338, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:177, and where b is greater than or equal to a + 14.	T68040, H17760, AA101036, AA129837
790775	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1600 of SEQ ID NO:178, b is an integer of 15 to 1614, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:178, and where b is greater than or equal to a + 14.	N25320, N31432, W81044, W81097
790888	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4278 of SEQ ID NO:179, b is an integer of 15 to 4292, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:179, and where b is greater than or	R14550, R15204, T26493, R21597, R22908, R23010, R41211, R41649, R43371, R41211, R41649, R43371, R58989, R59048, H05739, H05845, H17266, H17265, H23579, H44104, H46505, H47043, H58955, H59002, H73676, H73730, H80078, H82275, H82289, H82399, H82381, H97810, H98133, H98737, N23117, N24310, N25196, N25265, N27792, N28735, N29893, N33395, N33904, N36066, N36839, N42542, N46060, N51230, N59535, N67737,

	equal to $a + 14$ .	N73641, N78481, N78694, W03555, W15202, W52445, W52723, W95124, AA047257, AA057142, AA204699, AA251464, AA430598
791506	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 229 of SEQ ID NO:180, $b$ is an integer of 15 to 243, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:180, and where $b$ is greater than or equal to $a + 14$ .	
791649	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 799 of SEQ ID NO:181, $b$ is an integer of 15 to 813, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:181, and where $b$ is greater than or equal to $a + 14$ .	
791802	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 808 of SEQ ID NO:182, $b$ is an integer of 15 to 822, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:182, and where $b$ is greater than or equal to $a + 14$ .	
792002	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 1081 of SEQ ID NO:183, $b$ is an integer of 15 to 1095, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:183, and where $b$ is greater than or equal to $a + 14$ .	T49735, T49736, T95310, T95391, T99384, T99612, R63493, R63494, H27739, R91698, R92136, H52608, H57619, H58464, H61415, H62139, H69019, H87167, H87669, N21358, N70307, N79596, W19063, W58498, W58651, W79687, W81289, AA099849, AA099972, AA232767
792291	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer	T55436, R21797, R22403, R22452, R22916, R23020, R76901, R77068, H22573, H25752, H25866, R83900, H50717, H50821, H64026, H64791, H95702, N64545, N69769, N74704, N80341, W05092, W79489, W79634,

	between 1 to 3661 of SEQ ID NO:184, b is an integer of 15 to 3675, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:184, and where b is greater than or equal to a + 14.	AA005055, AA005007, AA025043, AA036711, AA037127, AA043916, AA055100, AA063627, AA069142, AA069230, AA069323, AA069376, AA112277, AA112531, AA115279, AA151238, AA151239, AA151582, AA149398, AA149961, AA150069, AA158029, AA158321, AA158692, AA158693, AA161232, AA236787, AA236834, AA256776, AA261961
792371	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1026 of SEQ ID NO:185, b is an integer of 15 to 1040, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:185, and where b is greater than or equal to a + 14.	
792660	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 803 of SEQ ID NO:186, b is an integer of 15 to 817, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:186, and where b is greater than or equal to a + 14.	T59054, T86590, T83271, R48677, R53483, R53482, R62329, R62330, R66651, R67372, R69095, R69210, R71144, R82632, R82676, H15764, H15765, H19518, H19605, H27898, H42872, H42936, H49329, H49330, H50062, H50061, H87268, H87324, H96667, N22675, N92574, W37223, W37563, W38866, W61119, W65380, AA035095, AA035635, AA037254, AA054951, AA062973, AA082301, AA132472
792782	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1066 of SEQ ID NO:187, b is an integer of 15 to 1080, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:187, and where b is greater than or equal to a + 14.	
792890	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1272 of SEQ ID NO:188, b is an integer of 15 to 1286, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:188, and where b is greater than or equal to a + 14.	AA251351

792931	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1724 of SEQ ID NO:189, b is an integer of 15 to 1738, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:189, and where b is greater than or equal to a + 14.	
792943	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1909 of SEQ ID NO:190, b is an integer of 15 to 1923, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:190, and where b is greater than or equal to a + 14.	
793104	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 236 of SEQ ID NO:191, b is an integer of 15 to 250, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:191, and where b is greater than or equal to a + 14.	
793445	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1888 of SEQ ID NO:192, b is an integer of 15 to 1902, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:192, and where b is greater than or equal to a + 14.	AA034998, AA044249, AA088830, AA429418
793446	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 546 of SEQ ID NO:193, b is an integer of 15 to 560, where both a and b correspond to the positions of	T57765, T60664, H01264, H45774, H54790, H54842, H64484, H64485, N98810, W58332, W58653, W74582, W79320, W79420, W79565, W92452, AA027210, AA027209, AA029725, AA029663, AA088693, AA121506, AA127731, AA428362

	nucleotide residues shown in SEQ ID NO:193, and where b is greater than or equal to a + 14.	
793639	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 576 of SEQ ID NO:194, b is an integer of 15 to 590, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:194, and where b is greater than or equal to a + 14.	N69881, N93023, N98853, W21375, W73944, W77988, AA169530, AA169837, AA176453, AA176931
794213	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 677 of SEQ ID NO:195, b is an integer of 15 to 691, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:195, and where b is greater than or equal to a + 14.	N53897, N55318
795858	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1758 of SEQ ID NO:196, b is an integer of 15 to 1772, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:196, and where b is greater than or equal to a + 14.	
795955	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 661 of SEQ ID NO:197, b is an integer of 15 to 675, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:197, and where b is greater than or equal to a + 14.	
796359	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	

	between 1 to 543 of SEQ ID NO:198, b is an integer of 15 to 557, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:198, and where b is greater than or equal to a + 14.	
796555	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2597 of SEQ ID NO:199, b is an integer of 15 to 2611, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:199, and where b is greater than or equal to a + 14.	T69136, T69194, T95612, T95713, R53091, R73126, N41876, N49174, W05348, W04725, W31397, W31827, W92674, AA039513
796675	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2302 of SEQ ID NO:200, b is an integer of 15 to 2316, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:200, and where b is greater than or equal to a + 14.	
796743	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1133 of SEQ ID NO:201, b is an integer of 15 to 1147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:201, and where b is greater than or equal to a + 14.	
796792	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 674 of SEQ ID NO:202, b is an integer of 15 to 688, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:202, and where b is greater than or equal to a + 14.	
799668	Preferably excluded from the present invention are one or more	



	polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 290 of SEQ ID NO:203, b is an integer of 15 to 304, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:203, and where b is greater than or equal to a + 14.	
799669	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 403 of SEQ ID NO:204, b is an integer of 15 to 417, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:204, and where b is greater than or equal to a + 14.	
799673	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 537 of SEQ ID NO:205, b is an integer of 15 to 551, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:205, and where b is greater than or equal to a + 14.	
799674	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1087 of SEQ ID NO:206, b is an integer of 15 to 1101, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:206, and where b is greater than or equal to a + 14.	
799678	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 501 of SEQ ID NO:207, b is an integer of 15 to 515, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:207, and where b is greater than or	

	equal to $a + 14$ .	
799728	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 255 of SEQ ID NO:208, $b$ is an integer of 15 to 269, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:208, and where $b$ is greater than or equal to $a + 14$ .	
799748	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 720 of SEQ ID NO:209, $b$ is an integer of 15 to 734, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:209, and where $b$ is greater than or equal to $a + 14$ .	H19497, H19579, H50117, H50164, H52826, H52827, H61184, H62087, H96290, H96291, N20586, N21261, N28978, N30137, N30490, N35750, W31933, W37535, N90542, AA418545, AA418511
799760	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 644 of SEQ ID NO:210, $b$ is an integer of 15 to 658, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:210, and where $b$ is greater than or equal to $a + 14$ .	
799805	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 190 of SEQ ID NO:211, $b$ is an integer of 15 to 204, where both $a$ and $b$ correspond to the positions of nucleotide residues shown in SEQ ID NO:211, and where $b$ is greater than or equal to $a + 14$ .	
800296	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$ , where $a$ is any integer between 1 to 1257 of SEQ ID NO:212, $b$ is an integer of 15 to 1271, where both	

	a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:212, and where b is greater than or equal to a + 14.	
800327	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1011 of SEQ ID NO:213, b is an integer of 15 to 1025, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:213, and where b is greater than or equal to a + 14.	
800816	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 337 of SEQ ID NO:214, b is an integer of 15 to 351, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:214, and where b is greater than or equal to a + 14.	
800835	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1073 of SEQ ID NO:215, b is an integer of 15 to 1087, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:215, and where b is greater than or equal to a + 14.	
805429	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1963 of SEQ ID NO:216, b is an integer of 15 to 1977, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:216, and where b is greater than or equal to a + 14.	
805458	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	T82438, T82439, R19121, R20391, R28602, R36743, R43508, R46035, R43508, R46035, R79588, H24625, N28372, N28785, N29421, N35476, N57353, N72836, N79096, W03034,

	formula of a-b, where a is any integer between 1 to 2801 of SEQ ID NO:217, b is an integer of 15 to 2815, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:217, and where b is greater than or equal to a + 14.	AA016073, AA019733, AA021030, AA062895, AA081968, AA115692, AA133511, AA151852, AA149707, AA194903, AA194902
805478	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1631 of SEQ ID NO:218, b is an integer of 15 to 1645, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:218, and where b is greater than or equal to a + 14.	
805805	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 464 of SEQ ID NO:219, b is an integer of 15 to 478, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:219, and where b is greater than or equal to a + 14.	
806486	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 818 of SEQ ID NO:220, b is an integer of 15 to 832, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:220, and where b is greater than or equal to a + 14.	
806498	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1878 of SEQ ID NO:221, b is an integer of 15 to 1892, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:221, and where b is greater than or equal to a + 14.	
806819	Preferably excluded from the present	

	invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 854 of SEQ ID NO:222, b is an integer of 15 to 868, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:222, and where b is greater than or equal to a + 14.	
810870	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1502 of SEQ ID NO:223, b is an integer of 15 to 1516, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:223, and where b is greater than or equal to a + 14.	R50267, R50730, H27672, H27673, H30138, H99256, N74342, N80868, W05054, W07601
811730	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1292 of SEQ ID NO:224, b is an integer of 15 to 1306, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:224, and where b is greater than or equal to a + 14.	
813025	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 570 of SEQ ID NO:225, b is an integer of 15 to 584, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:225, and where b is greater than or equal to a + 14.	
813233	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 509 of SEQ ID NO:226, b is an integer of 15 to 523, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID	

	NO:226, and where b is greater than or equal to a + 14.	
813262	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2363 of SEQ ID NO:227, b is an integer of 15 to 2377, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:227, and where b is greater than or equal to a + 14.	
815637	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 449 of SEQ ID NO:228, b is an integer of 15 to 463, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:228, and where b is greater than or equal to a + 14.	
815853	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1218 of SEQ ID NO:229, b is an integer of 15 to 1232, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:229, and where b is greater than or equal to a + 14.	R53293, R59708, R59818, R88929, R89609, H78819, N52182, AA125808, AA128281
815999	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1049 of SEQ ID NO:230, b is an integer of 15 to 1063, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:230, and where b is greater than or equal to a + 14.	
823427	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1049 of SEQ ID NO:231.	T53986, T60846, T72425, R18752, H22479, H50211, N40817, N93431, W21474, W21308, W32281, W44860, W95821, N90881, AA132037, AA131965, AA151157, AA155868, AA156600, AA156837, AA157061, AA157045, AA160623, AA169460, AA176447, AA178894,

	b is an integer of 15 to 1063, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:231, and where b is greater than or equal to a + 14.	AA179764, AA180438, AA181145, AA181144, AA196382, AA196478
823704	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1460 of SEQ ID NO:232, b is an integer of 15 to 1474, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:232, and where b is greater than or equal to a + 14.	
824798	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1768 of SEQ ID NO:233, b is an integer of 15 to 1782, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:233, and where b is greater than or equal to a + 14.	
825018	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2194 of SEQ ID NO:234, b is an integer of 15 to 2208, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:234, and where b is greater than or equal to a + 14.	
825076	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2566 of SEQ ID NO:235, b is an integer of 15 to 2580, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:235, and where b is greater than or equal to a + 14.	
825787	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	

	sequence described by the general formula of a-b, where a is any integer between 1 to 2994 of SEQ ID NO:236, b is an integer of 15 to 3008, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:236, and where b is greater than or equal to a + 14.	
826116	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 863 of SEQ ID NO:237, b is an integer of 15 to 877, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:237, and where b is greater than or equal to a + 14.	
826147	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3025 of SEQ ID NO:238, b is an integer of 15 to 3039, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:238, and where b is greater than or equal to a + 14.	
827020	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1978 of SEQ ID NO:239, b is an integer of 15 to 1992, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:239, and where b is greater than or equal to a + 14.	
827586	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 483 of SEQ ID NO:240, b is an integer of 15 to 497, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:240, and where b is greater than or equal to a + 14.	



827732	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 302 of SEQ ID NO:241, b is an integer of 15 to 316, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:241, and where b is greater than or equal to a + 14.	
827735	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 815 of SEQ ID NO:242, b is an integer of 15 to 829, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14.	
827740	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 824 of SEQ ID NO:243, b is an integer of 15 to 838, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:243, and where b is greater than or equal to a + 14.	R21513, R22316, R42033, R43706, R42033, R43706, R63113, R70954, R71006, N48618, N53377, AA912400
827808	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2839 of SEQ ID NO:244, b is an integer of 15 to 2853, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:244, and where b is greater than or equal to a + 14.	
828251	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1183 of SEQ ID NO:245, b is an integer of 15 to 1197, where both a and b correspond to the positions of	

	nucleotide residues shown in SEQ ID NO:245, and where b is greater than or equal to a + 14.	
828357	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 834 of SEQ ID NO:246, b is an integer of 15 to 848, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:246, and where b is greater than or equal to a + 14.	
828449	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1322 of SEQ ID NO:247, b is an integer of 15 to 1336, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:247, and where b is greater than or equal to a + 14.	
828612	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1062 of SEQ ID NO:248, b is an integer of 15 to 1076, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:248, and where b is greater than or equal to a + 14.	R28513, R28661, R31336, R41867, R41867, R60004, H19945, H19946, H22061, H46271, H46342, H82619, H82618, N20678, W96169, AA010842, AA278855, AA582295, AA583721, AA639735, AA579409, AA568321, AA833752, AA907437, AI054389, W22584
828647	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2411 of SEQ ID NO:249, b is an integer of 15 to 2425, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:249, and where b is greater than or equal to a + 14.	
828698	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	

	between 1 to 1394 of SEQ ID NO:250, b is an integer of 15 to 1408, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:250, and where b is greater than or equal to a + 14.	
828962	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 480 of SEQ ID NO:251, b is an integer of 15 to 494, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:251, and where b is greater than or equal to a + 14.	
828982	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2477 of SEQ ID NO:252, b is an integer of 15 to 2491, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:252, and where b is greater than or equal to a + 14.	T64550, T65973, T94849, T94894, R07359, R07409, R34782, R35670, R35781, R56137, R56532, R64039, R66397, R67131, H01215, H02256, H02354, H03227, H04019, R94572, R94573, H51242, H60286, H65939, H72416, H72857, N22537, N24628, N24936, N33813, N35712, N35830, N35916, N43982, N51363, N64462, N70838, N75470, N75760, W01444, W05279, W57605, W58752, W72612, W72970, W73260, W73535, W76678, W76207, W94918, W91971, W92319, W92355, AA024690, AA024643, AA028083, AA028084, AA028169, AA035743, AA045830, AA045917, AA081723, AA086310, AA085740, AA102651, AA101305, AA126788, AA126837, AA126865, AA127295, AA129688, AA129664, AA133503, AA133504, AA132801, AA134537, AA134547, AA186712, AA188264, AA215597, AA463977, AA464112, AA417286, AA417312, AA259228, AA279952, AA287814, AA468227, AA468302, AA526480, AA553703, AA587072, AA635683, AA639361, AA573471, AA579754, AA579812, AA580600, AA730425, AA741436, AA804629, AA829189, AA830255, AA865594, AA885821, AA918979, AA962033, AA985542, AA985571, AA987607, AA995783, A1075334, D79160, N84712, N88655, C03235, AA094028
829282	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1111 of SEQ ID NO:253, b is an integer of 15 to 1125, where both a and b correspond to the positions of	

	nucleotide residues shown in SEQ ID NO:253, and where b is greater than or equal to a + 14.	
829368	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1395 of SEQ ID NO:254, b is an integer of 15 to 1409, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:254, and where b is greater than or equal to a + 14.	R61547, R76124, H01565, H02950, H04248, H29996, H99672, W19970
829751	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 476 of SEQ ID NO:255, b is an integer of 15 to 490, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:255, and where b is greater than or equal to a + 14.	
829773	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1219 of SEQ ID NO:256, b is an integer of 15 to 1233, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:256, and where b is greater than or equal to a + 14.	T96982, T97094, H53488, H53861, H64894, H65486, N62304, N67480, N78709, W03409, W07598, W73770, AA025496, AA025812, AA133948
829934	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2390 of SEQ ID NO:257, b is an integer of 15 to 2404, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:257, and where b is greater than or equal to a + 14.	
829942	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	T64541, T65964, R01423, R01424, R05277, R19450, R44699, R51779, R51780, R44699, H11322, H11349, H13859, H13911, H21393, H21437, H21890, H22117, H45982, H46047, H47137, R98886, H54491, H54854, H98744,

	between 1 to 2078 of SEQ ID NO:258, b is an integer of 15 to 2092, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:258, and where b is greater than or equal to a + 14.	N23465, N37080, N46155, N46396, N58995, N62715, N93640, W60228, W60227, W74349, W76544, W87768, W87883, W90517, W90518, AA010775, AA011055, AA029083, AA029084, AA036822, AA057660, AA075916, AA082814, AA101057, AA130702, AA132788, AA133063, AA147813, AA148063, AA151487, AA151511, AA173298, AA173348, AA181036, AA187993, AA187994, AA192370, AA192357, AA243010, AA243264, AA250948
829951	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 373 of SEQ ID NO:259, b is an integer of 15 to 387, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:259, and where b is greater than or equal to a + 14.	
830173	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3698 of SEQ ID NO:260, b is an integer of 15 to 3712, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:260, and where b is greater than or equal to a + 14.	T52493, T52572, T56913, T61268, T61320, T70063, T70130, T72005, T87844, T94182, T70248, R24534, R24639, R31200, R64161, R64274, R70751, R70750, H16189, H89274, H99749, N25430, N25537, N32578, N32816, N34120, N34134, N34491, N35081, N42260, N43821, N62152, N62798, N64065, N64169, N67362, N69808, N74678, N93912, N49165, W04704, W05040, W16565, W19920, W31806, W31907, W37354, W37355, W40493, W45266, W45455, W52925, W58628, W92222, W92345, N91265, AA027083, AA027124, AA028969, AA029137, AA029257, AA083657, AA084297, AA121151, AA121131, AA126957, AA127166, AA128353, AA128495, AA128834, AA132690, AA132783, AA136553, AA152414, AA150706, AA150808, AA156272, AA164766, AA164767, AA171427, AA171794, AA173592, AA173949, AA190421, AA190580, AA191383, AA224415, AA232135
830200	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 883 of SEQ ID NO:261, b is an integer of 15 to 897, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:261, and where b is greater than or equal to a + 14.	AA524284, AA662477, AA887924

830365	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1891 of SEQ ID NO:262, b is an integer of 15 to 1905, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:262, and where b is greater than or equal to a + 14.	R42905, R59718, R62419, R72182, R72228, H22520, H22519, H25889, H45643, H46451, H46992, H84483, N50834, N92573, AA022699, AA022791, AA037734, AA037735, AA040585, AA040557, AA047816, AA159187, AA159282, AA223337, AA505391, AA515591, AA524466, AA613383, AA627298, AA578816, AA769153, AA826456, AA830896, AA831083, AA837917, AA977053, A1083822, A1090301, A1084104
830456	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1410 of SEQ ID NO:263, b is an integer of 15 to 1424, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:263, and where b is greater than or equal to a + 14.	T39800, T39875, T40331, T80148, R01135, R05754, R12866, R15287, R21703, R39361, H00652, H00741, H05366, H17706, H23423, R97800, R97849, N25478, N41797, N48511, N98906, W19893, W23945, W35174, W60540, W78229, W79282, W84685, AA022952, AA026821, AA026953, AA074956, AA075111, AA114974, AA114988, AA192860, AA193064
830549	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1273 of SEQ ID NO:264, b is an integer of 15 to 1287, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:264, and where b is greater than or equal to a + 14.	R60171, H26796, H96303, N91699, W25137, AA069218, AA088565, AA161178
830602	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 977 of SEQ ID NO:265, b is an integer of 15 to 991, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:265, and where b is greater than or equal to a + 14.	
830610	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2306 of SEQ ID NO:266, b is an integer of 15 to 2320, where both a and b correspond to the positions of	

	nucleotide residues shown in SEQ ID NO:266, and where b is greater than or equal to a + 14.	
830644	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 409 of SEQ ID NO:267, b is an integer of 15 to 423, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:267, and where b is greater than or equal to a + 14.	
830707	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1832 of SEQ ID NO:268, b is an integer of 15 to 1846, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:268, and where b is greater than or equal to a + 14.	
830709	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 587 of SEQ ID NO:269, b is an integer of 15 to 601, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:269, and where b is greater than or equal to a + 14.	
830733	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 866 of SEQ ID NO:270, b is an integer of 15 to 880, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:270, and where b is greater than or equal to a + 14.	T26638, R49962, H96664, N71762, N90691, AA040156, AA128271, AA418045, AA418216, AA535799, AA583405, AA768811
830768	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	

	between 1 to 2470 of SEQ ID NO:271, b is an integer of 15 to 2484, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:271, and where b is greater than or equal to a + 14.	
830855	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 737 of SEQ ID NO:272, b is an integer of 15 to 751, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:272, and where b is greater than or equal to a + 14.	H17127, AA100311, AA112910, AA282249, AA578649, AA748590
830949	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3295 of SEQ ID NO:273, b is an integer of 15 to 3309, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:273, and where b is greater than or equal to a + 14.	
830965	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 829 of SEQ ID NO:274, b is an integer of 15 to 843, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:274, and where b is greater than or equal to a + 14.	
830973	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2014 of SEQ ID NO:275, b is an integer of 15 to 2028, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:275, and where b is greater than or equal to a + 14.	
830979	Preferably excluded from the present invention are one or more	



	polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1441 of SEQ ID NO:276, b is an integer of 15 to 1455, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:276, and where b is greater than or equal to a + 14.	
830989	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1909 of SEQ ID NO:277, b is an integer of 15 to 1923, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:277, and where b is greater than or equal to a + 14.	
831134	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1366 of SEQ ID NO:278, b is an integer of 15 to 1380, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:278, and where b is greater than or equal to a + 14.	
831200	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1004 of SEQ ID NO:279, b is an integer of 15 to 1018, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:279, and where b is greater than or equal to a + 14.	
831260	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1178 of SEQ ID NO:280, b is an integer of 15 to 1192, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:280, and where b is greater than or	R15008, R28066, R68324, H20638, N25438, N67982, N67983, N67999, N68004, N68005, N80403, N80423, N80429, N80430, AA024581, AA024582, AA024637, AA862760, AA091142

	equal to $a + 14$ .	
831531	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1741 of SEQ ID NO:281, b is an integer of 15 to 1755, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:281, and where b is greater than or equal to $a + 14$ .	T66624, R16038, R26139, R26353, H15795, H16285, H21749, H21945, H22698, H23978, H52286, H52523, H60184, H60227, H68044, H81748, H81749, N46859, N47179, N51722, N51808, AA031701, AA031866, AA043760, AA043761, AA081005, AA081148, AA195519, AA470636, AA534463, AA555198, AA631348, AA721036, AA737025, AA761301, AA764993, AA765314, AA765749, AA878422, U47720, C21223
831665	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1079 of SEQ ID NO:282, b is an integer of 15 to 1093, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:282, and where b is greater than or equal to $a + 14$ .	
831724	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1542 of SEQ ID NO:283, b is an integer of 15 to 1556, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:283, and where b is greater than or equal to $a + 14$ .	R52161, N45179, N68350, N94021, W02782, W24840, W61323, AA907441
831884	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1015 of SEQ ID NO:284, b is an integer of 15 to 1029, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:284, and where b is greater than or equal to $a + 14$ .	
831897	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1569 of SEQ ID NO:285, b is an integer of 15 to 1583, where both	AA056348, AA127534

	a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:285, and where b is greater than or equal to a + 14.	
831922	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1163 of SEQ ID NO:286, b is an integer of 15 to 1177, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:286, and where b is greater than or equal to a + 14.	
831963	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 492 of SEQ ID NO:287, b is an integer of 15 to 506, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:287, and where b is greater than or equal to a + 14.	
832074	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 934 of SEQ ID NO:288, b is an integer of 15 to 948, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:288, and where b is greater than or equal to a + 14.	
832266	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1020 of SEQ ID NO:289, b is an integer of 15 to 1034, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:289, and where b is greater than or equal to a + 14.	T70612, T70879, H13555, H23264, R97792, R97842, N75850, W07434, W19866, N90056, AA043395, AA463232, AA463231
832309	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	

	formula of a-b, where a is any integer between 1 to 3077 of SEQ ID NO:290, b is an integer of 15 to 3091, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:290, and where b is greater than or equal to a + 14.	
832342	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 504 of SEQ ID NO:291, b is an integer of 15 to 518, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:291, and where b is greater than or equal to a + 14.	
832351	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 484 of SEQ ID NO:292, b is an integer of 15 to 498, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:292, and where b is greater than or equal to a + 14.	
832352	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 455 of SEQ ID NO:293, b is an integer of 15 to 469, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:293, and where b is greater than or equal to a + 14.	
832434	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 654 of SEQ ID NO:294, b is an integer of 15 to 668, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:294, and where b is greater than or equal to a + 14.	
832490	Preferably excluded from the present	T86496, H24346, R84505, N26874, N98621,

	invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1386 of SEQ ID NO:295, b is an integer of 15 to 1400, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14.	W04678, W04692, W24267, W93387, W94971, AA036953, AA136869, AA136799, AA147214, AA160413, AA535592, AA931261, AA931403, AA962726, AA992456
832573	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 946 of SEQ ID NO:296, b is an integer of 15 to 960, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14.	
832580	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 643 of SEQ ID NO:297, b is an integer of 15 to 657, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14.	
833394	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 878 of SEQ ID NO:298, b is an integer of 15 to 892, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:298, and where b is greater than or equal to a + 14.	
835355	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1610 of SEQ ID NO:299, b is an integer of 15 to 1624, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID	AA076638, AA916592, AI088936, AI089690

	NO:299, and where b is greater than or equal to a + 14.	
835497	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1955 of SEQ ID NO:300, b is an integer of 15 to 1969, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:300, and where b is greater than or equal to a + 14.	
835728	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1868 of SEQ ID NO:301, b is an integer of 15 to 1882, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:301, and where b is greater than or equal to a + 14.	
835978	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2790 of SEQ ID NO:302, b is an integer of 15 to 2804, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:302, and where b is greater than or equal to a + 14.	
836091	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3845 of SEQ ID NO:303, b is an integer of 15 to 3859, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:303, and where b is greater than or equal to a + 14.	R02093, R02205, R02336, R02439, R19436, R44685, R44685, R72354, H10160, H49884, H49885, N23208, N28789, N29901, N42953, N55093, N77305, N99373, W46396, W46504, AA082311, AA176281, AA176282, AA227971, AA228079, AA234964, AA234145, AA281787, AA281656, AA524468, AA551888, AA631173, AA639499, AA811344, AA830439, AA831974, AA923665, C03439, AA641655, AA091346, AA400968, AA400884
836274	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3364 of SEQ ID NO:304,	T75442, R20393, R43511, R43511, R73650, R73731, R80152, R80886, H97932, H98616, N33018, N71679, N99650, AA001053, AA001089, AA044947, AA044943, AA149057, AA464856, AA427892, AA228265, AA230021, AA482694, AA483691, AA484850, AA513037,

	b is an integer of 15 to 3378, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:304, and where b is greater than or equal to a + 14.	AA516076, AA532381, AA583355, AA618566, AA577028, AA730651, AA730790, AA745667, AA829807, AA923038, AA931937, AA932867, AA934400, AA934413, AA971551, AA971743, AA972772, AA977253, AA992454, AA994794, AI089906, AI094921, D79281, C06099, D44840, C20741, AA283186, AA292346, AA394164
836731	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1000 of SEQ ID NO:305, b is an integer of 15 to 1014, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:305, and where b is greater than or equal to a + 14.	
838014	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2113 of SEQ ID NO:306, b is an integer of 15 to 2127, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:306, and where b is greater than or equal to a + 14.	
838874	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 652 of SEQ ID NO:307, b is an integer of 15 to 666, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:307, and where b is greater than or equal to a + 14.	R61165, N44200
839120	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2157 of SEQ ID NO:308, b is an integer of 15 to 2171, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:308, and where b is greater than or equal to a + 14.	T74462, R18264, H23432, AA279685, AA847441, AA904076, AA393782

839611	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 6149 of SEQ ID NO:309, b is an integer of 15 to 6163, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:309, and where b is greater than or equal to a + 14.	T93695, T93696, T96161, R32227, R32254, R32304, R33503, R34044, R71178, H93366, N50709, N55039, AA165143, AA199856, AA199927, AA234331, AA262892, AA423987, AA423986, AA525886, AA661602, AA731504, AA741228, AA814795, AA828858, AA829196, AA831198, AA834822, AA865590, AA886436, AA903649, D82270, D82453, D82464, AA642466, AA219620, AA219628, AA400707, AA400674, AA421941, AA633988, AA663219, AA663250, AA665538, AA724260, AI074714, T26891, T26926
840138	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2072 of SEQ ID NO:310, b is an integer of 15 to 2086, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:310, and where b is greater than or equal to a + 14.	
840616	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2149 of SEQ ID NO:311, b is an integer of 15 to 2163, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:311, and where b is greater than or equal to a + 14.	
840780	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1383 of SEQ ID NO:312, b is an integer of 15 to 1397, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:312, and where b is greater than or equal to a + 14.	
840857	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4092 of SEQ ID NO:313, b is an integer of 15 to 4106, where both	T50389, T50520, T55419, T55495, T55974, T57220, R34591, R34592, R69726, H21148, R85777, R99233, H61311, H62351, H85185, H88299, N23288, N32662, N58504, N78093, N92665, N99611, AA005068, AA007333, AA007334, AA036884, AA044715, AA045458, AA046500, AA045654, AA115936, AA121004,



	a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:313, and where b is greater than or equal to a + 14.	AA126775, AA133605, AA133606, AA133980, AA181633, AA182611, AA232979, AA233365, AA459953, AA460042, AA282826, AA285050, AA506082, AA558006, AA601060, AA767799, AA804323, AA807029, AA807087, AA825536, AA833810, AA922732, AA928638, AA960990, N56482, N62047, W27456, W26569, AA092778, AA652535, AA065256, AA065257, AA450197, AA452846, AA452986, AA705224, Z19460, AA884767, AA969488, AA977494, AI002996, AI032008, Z28526, D20112, T19336
840862	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 518 of SEQ ID NO:314, b is an integer of 15 to 532, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:314, and where b is greater than or equal to a + 14.	T94528, N40545, N46592, N92934, AA570273, AA873604, AA910827, AA932397, AA971868, AI095210, N56229, AA648290, F20835, AA629912
840864	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1924 of SEQ ID NO:315, b is an integer of 15 to 1938, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:315, and where b is greater than or equal to a + 14.	R40870, R44820, H26640, W78814, W80713, AA195492, AA937549, AI085492, AI094865, AA449317, AA884600, AA909529, AA923452, AA971781, AI084795, AI089007, AA702758, AA702769
840936	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 804 of SEQ ID NO:316, b is an integer of 15 to 818, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:316, and where b is greater than or equal to a + 14.	
840938	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 823 of SEQ ID NO:317, b is an integer of 15 to 837, where both a and b correspond to the positions of	

	nucleotide residues shown in SEQ ID NO:317, and where b is greater than or equal to a + 14.	
841884	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1434 of SEQ ID NO:318, b is an integer of 15 to 1448, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:318, and where b is greater than or equal to a + 14.	
842241	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1479 of SEQ ID NO:319, b is an integer of 15 to 1493, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:319, and where b is greater than or equal to a + 14.	
843712	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 595 of SEQ ID NO:320, b is an integer of 15 to 609, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:320, and where b is greater than or equal to a + 14.	R02291, N94598, W85882, AA255975
844040	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 488 of SEQ ID NO:321, b is an integer of 15 to 502, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:321, and where b is greater than or equal to a + 14.	W24428, AA143434, AA459809
844336	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer	

	between 1 to 2616 of SEQ ID NO:322, b is an integer of 15 to 2630, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:322, and where b is greater than or equal to a + 14.	
844612	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1860 of SEQ ID NO:323, b is an integer of 15 to 1874, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:323, and where b is greater than or equal to a + 14.	
844617	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2311 of SEQ ID NO:324, b is an integer of 15 to 2325, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:324, and where b is greater than or equal to a + 14.	
845251	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 771 of SEQ ID NO:325, b is an integer of 15 to 785, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:325, and where b is greater than or equal to a + 14.	T68474, AA159183, AA464447, AA424290, AA424487, AA631793, AA928390, AA946921, AA975194, AA977141, AA430527, AA430612, AA477798
845764	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 230 of SEQ ID NO:326, b is an integer of 15 to 244, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:326, and where b is greater than or equal to a + 14.	
846187	Preferably excluded from the present invention are one or more	

<p>polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2440 of SEQ ID NO:327, b is an integer of 15 to 2454, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:327, and where b is greater than or equal to a + 14.</p>	
--	--

#### *Polynucleotide and Polypeptide Variants*

The present invention is directed to variants of the polynucleotide sequence disclosed in SEQ ID NO:X or the complementary strand thereto, and/or the cDNA sequence contained in a cDNA clone contained in the deposit.

5       The present invention also encompasses variants of the breast, ovarian, breast cancer and/or ovarian cancer polypeptide sequence disclosed in SEQ ID NO:Y, a polypeptide sequence encoded by the polynucleotide sequence in SEQ ID NO:X, and/or a polypeptide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

10       "Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

15       The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence of the related cDNA contained in a deposited library or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA in the related cDNA contained in a deposited library, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polypeptides encoded by these nucleic acid molecules are also encompassed by the invention. In another embodiment, the invention encompasses nucleic acid molecules which comprise or alternatively consist of, a polynucleotide which hybridizes under stringent hybridization conditions, or alternatively, under low stringency conditions, to the nucleotide coding sequence in SEQ ID NO:X, the

20

25

nucleotide coding sequence of the related cDNA clone contained in a deposited library, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA in the related cDNA clone contained in a deposited library, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

The present invention is also directed to polypeptides which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to, for example, the polypeptide sequence shown in SEQ ID NO:Y, a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the cDNA in the related cDNA clone contained in a deposited library, and/or polypeptide fragments of any of these polypeptides (e.g., those fragments described herein). Polynucleotides which hybridize to the complement of the nucleic acid molecules encoding these polypeptides under stringent hybridization conditions, or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be, for example, an entire sequence referred to in Table 1, an ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of

the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the  
5 algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining  
10 Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results.  
15 This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a  
20 nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment,  
25 which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at  
30 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases

were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence in SEQ ID NO:Y or a fragment thereof, the amino acid sequence encoded by the nucleotide sequence in SEQ ID NO:X or a fragment thereof, or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library, or a fragment thereof, can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci.6:237- 245(1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window

Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results.

5 This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject  
10 residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues  
15 to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C- terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue  
20 query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the  
25 FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected.  
30 Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the



purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which less than 50, less than 40, less than 30, less than 20, less than 10, or 5-50, 5-25, 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, as discussed herein, one or more amino acids can be deleted from the N-terminus or C-terminus of the polypeptide of the present invention without substantial loss of biological function. The authors of Ron et al., *J. Biol. Chem.* 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., *J. Biotechnology* 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (*J. Biol. Chem.* 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that

"[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

5        Furthermore, as discussed herein, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are  
10       removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

      Thus, the invention further includes polypeptide variants which show a functional activity (e.g., biological activity) of the polypeptide of the invention of which they are a  
15       variant. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity.

      The present application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein or fragments thereof, (e.g., including but not limited to fragments encoding a polypeptide  
20       having the amino acid sequence of an N and/or C terminal deletion), irrespective of whether they encode a polypeptide having functional activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid  
25       molecules of the present invention that do not encode a polypeptide having functional activity include, inter alia, (1) isolating a gene or allelic or splice variants thereof in a cDNA library; (2) in situ hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the gene, as described in Verma et al., Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York (1988); and (3) Northern Blot  
30       analysis for detecting mRNA expression in specific tissues.

      Preferred, however, are nucleic acid molecules having sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed

herein, which do, in fact, encode a polypeptide having a functional activity of a polypeptide of the invention.

Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to, for example, the nucleic acid sequence of the cDNA in the related cDNA clone contained in a deposited library, the nucleic acid sequence referred to in Table 1 (SEQ ID NO:X), or fragments thereof, will encode polypeptides "having functional activity." In fact, since degenerate variants of any of these nucleotide sequences all encode the same polypeptide, in many instances, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.

For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells,

Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly. Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

A further embodiment of the invention relates to a polypeptide which comprises the amino acid sequence of a polypeptide having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30

amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions. Of course it is highly preferable for a polypeptide to have an amino acid sequence which comprises the amino acid sequence of a polypeptide of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, and/or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library which contains, in order of ever-increasing preference, at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid substitutions. In specific embodiments, the number of additions, substitutions, and/or deletions in the amino acid sequence of SEQ ID NO:Y or fragments thereof (e.g., the mature form and/or other fragments described herein), an amino acid sequence encoded by SEQ ID NO:X or fragments thereof, and/or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library or fragments thereof, is 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, conservative amino acid substitutions are preferable.

#### *Polynucleotide and Polypeptide Fragments*

The present invention is also directed to polynucleotide fragments of the breast, ovarian, breast cancer and/or ovarian cancer polynucleotides (nucleic acids) of the invention. In the present invention, a "polynucleotide fragment" refers, for example, to a polynucleotide having a nucleic acid sequence which: is a portion of the cDNA contained in a deposited cDNA clone; or is a portion of a polynucleotide sequence encoding the polypeptide encoded by the cDNA contained in a deposited cDNA clone; or is a portion of the polynucleotide sequence in SEQ ID NO:X or the complementary strand thereto; or is a polynucleotide sequence encoding a portion of the polypeptide of SEQ ID NO:Y; or is a polynucleotide sequence encoding a portion of a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto. The nucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, at least about 100 nt, at least about 125 nt or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from, for example, the sequence contained in the cDNA in a related cDNA clone contained in a deposited library, the nucleotide sequence shown in SEQ ID NO:X or the complementary stand thereto. In this context "about" includes the particularly recited value or a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides. These nucleotide fragments have uses that

include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., at least 150, 175, 200, 250, 500, 600, 1000, or 2000 nucleotides in length) are also encompassed by the invention.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, and 6151 to the end of SEQ ID NO:X, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity) of the polypeptide encoded by the polynucleotide of which the sequence is a portion. More preferably, these fragments can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides or fragments.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from

about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, and 6151 to the end of the cDNA nucleotide sequence contained in the deposited cDNA clone, or the complementary strand thereto. In this context "about" includes the particularly recited range, or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity) of the polypeptide encoded by the cDNA nucleotide sequence contained in the deposited cDNA clone. More preferably, these fragments can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these fragments under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides or fragments.

In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y, a portion of an amino acid sequence encoded by the polynucleotide sequence of SEQ ID NO:X, and/or encoded by the cDNA contained in the related cDNA clone contained in a deposited library. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region.

Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, an amino acid sequence from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, 1441-1460, 1461-1480, 1481-1500, 1501-1520, 1521-1540, 1541-1560, 1561-1580, 1581-1600, 1601-1620, 1621-1640, 1641-1660, 1661-1680, 1681-1700, 1701-1720, 1721-1740, 1741-1760, 1761-1780, 1781-1800, 1801-1820, 1821-1840, 1841-1860, 1861-1880, 1881-1900, 1901-1920, 1921-1940, 1941-1960, 1961-1980, and 1981 to the end of SEQ ID NO:Y. Moreover, polypeptide fragments of the invention may be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, or ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either terminus or at both termini. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

Even if deletion of one or more amino acids from the N-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example, the ability of shortened muteins to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptides generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the N-terminus. Whether a particular polypeptide lacking N-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted N-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.



Accordingly, polypeptide fragments of the invention include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

The present invention further provides polypeptides having one or more residues deleted from the amino terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, and/or a polypeptide encoded by the cDNA contained in the related cDNA clone contained in a deposited library). In particular, N-terminal deletions may be described by the general formula m-q, where q is a whole integer representing the total number of amino acid residues in a polypeptide of the invention (e.g., the polypeptide disclosed in SEQ ID NO:Y), and m is defined as any integer ranging from 2 to q-6. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example the ability of the shortened mutein to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

Accordingly, the present invention further provides polypeptides having one or more residues from the carboxy terminus of the amino acid sequence of a polypeptide disclosed

herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, and/or a polypeptide encoded by the cDNA contained in deposited cDNA clone referenced in Table 1). In particular, C-terminal deletions may be described by the general formula 1-n, where n is any whole integer ranging from 6 to q-1, and  
5 where n corresponds to the position of an amino acid residue in a polypeptide of the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

In addition, any of the above described N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides  
10 having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of a polypeptide encoded by SEQ ID NO:X (e.g., including, but not limited to, the preferred polypeptide disclosed as SEQ ID NO:Y), and/or the cDNA in the related cDNA clone contained in a deposited library, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also  
15 encompassed by the invention.

Any polypeptide sequence contained in the polypeptide of SEQ ID NO:Y, encoded by the polynucleotide sequences set forth as SEQ ID NO:X, or encoded by the cDNA in the related cDNA clone contained in a deposited library may be analyzed to determine certain preferred regions of the polypeptide. For example, the amino acid sequence of a polypeptide  
20 encoded by a polynucleotide sequence of SEQ ID NO:X, or the cDNA in a deposited cDNA clone may be analyzed using the default parameters of the DNASTAR computer algorithm (DNASTAR, Inc., 1228 S. Park St., Madison, WI 53715 USA; <http://www.dnastar.com/>).

Polypeptide regions that may be routinely obtained using the DNASTAR computer algorithm include, but are not limited to, Garnier-Robson alpha-regions, beta-regions,  
25 turn-regions, and coil-regions, Chou-Fasman alpha-regions, beta-regions, and turn-regions, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Eisenberg alpha- and beta-amphipathic regions, Karplus-Schulz flexible regions, Emini surface-forming regions and Jameson-Wolf regions of high antigenic index. Among highly preferred polynucleotides of the invention in this regard are those that encode polypeptides comprising regions that  
30 combine several structural features, such as several (e.g., 1, 2, 3 or 4) of the features set out above.

Additionally, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Emini surface-forming regions, and Jameson-Wolf regions of high antigenic index (i.e., containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) can routinely be used to determine polypeptide regions that exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from data by DNASTAR analysis by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

Preferred polypeptide fragments of the invention are fragments comprising, or alternatively consisting of, an amino acid sequence that displays a functional activity of the polypeptide sequence of which the amino acid sequence is a fragment.

By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

In preferred embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the antigenic fragments of the polypeptide of SEQ ID NO:Y, or portions thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Table 4

Sequence/ Contig ID	Epitope
508678	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 422 as residues: Gln-21 to Arg-43.
508968	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 423 as residues: Thr-1 to Lys-6.
509029	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 424 as residues: Asp-1 to Trp-8, Thr-12 to Cys-19, Pro-41 to Leu-51.
522632	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 426 as residues: Cys-69 to Asn-74, Lys-83 to Gly-89.
524655	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 427 as residues: Tyr-28 to Asn-35, Ile-45 to Lys-55.
525847	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 428 as residues: Lys-27 to Asp-33.
530306	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 429 as residues: Arg-1 to Arg-11, Tyr-21 to His-27.
532818	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 430 as residues: Pro-10 to Thr-21, Asp-32 to Thr-38, Gly-47 to Glu-60.
533385	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 431 as residues: Asn-17 to Trp-22, Pro-34 to Glu-49, His-61 to Ser-71.
533532	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 432 as residues: Glu-29 to Lys-37, Lys-110 to Ile-118, Arg-126 to Cys-135, Lys-157 to Gly-163, Gln-188 to Trp-201, Glu-269 to Thr-278.
534852	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 433 as residues: Gln-1 to Ser-14, Thr-23 to Val-31, Cys-43 to Ala-56, Glu-58 to Ser-96, Gly-101 to Tyr-109, Asn-143 to Tyr-148, Pro-154 to His-164, Ser-195 to Asn-201, Pro-264 to Pro-271.
537910	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 434 as residues: Pro-4 to Ala-11, Pro-110 to Arg-122.
539577	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 436 as residues: Pro-9 to Gln-19.
548595	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 439 as residues: Asp-27 to Asp-33, His-54 to Tyr-59, Ile-91 to Pro-96.
549337	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 440 as residues: Pro-38 to Asp-43, Arg-155 to Phe-162, Pro-164 to Asp-170, Pro-172 to Gly-182.
553091	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 442 as residues: Lys-55 to Lys-62, Gln-67 to Val-76, Lys-101 to Glu-111, Lys-125 to Arg-140, Arg-161 to Arg-166, Gln-171 to Asp-187.
553827	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 443 as residues: Glu-17 to Pro-22, Pro-70 to His-76, Thr-84 to Arg-92, Asp-109 to Tyr-117.
556350	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 444 as residues: Glu-1 to Ser-15, Phe-17 to Pro-22, Lys-116 to Arg-131.
556351	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 445 as residues: Gln-9 to Phe-23, Cys-53 to Ser-64, Glu-86 to Asp-93, Ile-100 to Glu-112, Tyr-124 to Glu-133, Ser-197 to Ser-204, Asn-208 to Glu-214, Lys-228 to Lys-233, Tyr-248 to Lys-259, Pro-330 to Ala-335, Gln-349 to Lys-355, Ala-365 to Glu-374, Ser-376 to Ser-397.
557007	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 446 as residues: Pro-46 to Tyr-54, Pro-81 to Gly-87, Pro-97 to Gly-104, Leu-106 to Asn-116, Asn-129 to Phe-134, Lys-147 to Tyr-158, Ala-192 to Ser-199, Asp-204 to Glu-215, Gly-221 to Ser-232.
558456	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 448 as

	residues: Glu-19 to Tyr-24, Ser-60 to Thr-65, Thr-82 to Pro-88.
558708	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 449 as residues: Arg-13 to Ala-20, Pro-27 to Arg-32, Lys-37 to Glu-62.
574789	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 450 as residues: Gly-16 to Lys-21.
578203	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 451 as residues: Thr-7 to Arg-18.
588869	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 453 as residues: Pro-14 to Ser-19, Glu-55 to Phe-60, Asp-93 to Ser-98, Thr-138 to Tyr-144, Asn-155 to Phe-163, Arg-168 to Ser-175, Gln-205 to Lys-210, Phe-226 to Thr-233.
597076	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 454 as residues: Ser-50 to Gln-56.
598656	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 455 as residues: Ser-85 to Tyr-92, Arg-109 to Lys-114.
614329	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 457 as residues: Arg-59 to Ala-67, Asn-78 to Arg-85.
620956	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 459 as residues: Ala-11 to Gln-16.
621889	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 460 as residues: Ser-84 to Gly-99, Pro-101 to Ser-112.
651784	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 462 as residues: Gly-29 to Gly-35, Ala-37 to Ala-48.
651826	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 463 as residues: Arg-1 to Ser-16, Gln-49 to Lys-60, Glu-77 to Leu-83, Gln-91 to Arg-100, Phe-140 to Ala-154, Asp-214 to Leu-219, Ala-258 to Met-275, Ile-289 to Lys-295, Ala-314 to Glu-320, Arg-327 to Met-332, Thr-383 to Ser-388, Ser-425 to Asp-433.
653282	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 464 as residues: Arg-12 to Ile-19, Glu-23 to Pro-29, Pro-37 to Val-45.
657122	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 465 as residues: Ala-6 to Gly-13, Arg-41 to Thr-47.
661442	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 466 as residues: Arg-6 to Ser-11, Asp-53 to Ser-59, Ala-88 to Ala-104, Thr-114 to Asn-121, Glu-128 to Val-137, Asn-144 to Thr-150, Ser-174 to Asn-180, Gly-203 to Asp-212.
664914	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 467 as residues: Pro-12 to Lys-17.
666654	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 468 as residues: Thr-5 to Leu-10, Pro-13 to Leu-24.
667084	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 469 as residues: Pro-1 to Pro-9, Gly-50 to Ser-55, Gly-80 to Ser-85, Gly-91 to Tyr-96, Arg-144 to Gln-160, Asp-195 to Thr-202, Lys-246 to Glu-252, Met-283 to Glu-288, Glu-292 to Glu-299, Ser-304 to Asn-310, Ala-356 to Tyr-362, Met-387 to Tyr-394, Gln-424 to Thr-431, Ser-450 to Arg-459.
667380	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 470 as residues: Pro-1 to Pro-6, Thr-134 to Gln-140, Tyr-142 to Arg-150.
671315	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 472 as residues: Ala-16 to Gly-21, Glu-28 to Gly-35.
671993	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 473 as residues: Pro-8 to Ser-23.
674618	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 474 as residues: Ile-3 to Ser-11, Arg-24 to Glu-30.
675027	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 475 as residues: His-47 to Ile-52, Ala-71 to Arg-76, Asp-78 to Lys-87.
677202	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 476 as residues: Val-45 to Gly-50, Thr-56 to Glu-64.
678504	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 477 as residues: Arg-7 to Ser-19.

678985	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 478 as residues: Lys-17 to Thr-23, Leu-26 to His-36, His-41 to Pro-56, Ala-60 to Gly-71, Lys-77 to Ser-91, Asp-101 to Lys-109, Asp-200 to Gly-206, Asp-245 to Leu-253, Gln-262 to Phe-274.
682161	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 479 as residues: Arg-5 to Pro-11, Pro-22 to Thr-29, Trp-53 to Arg-62, Pro-69 to Gly-78, Lys-98 to Tyr-103, Glu-144 to His-151, Pro-172 to Leu-178, Gln-193 to Glu-200.
683476	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 480 as residues: Ala-5 to Trp-19.
693589	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 482 as residues: Cys-1 to Arg-13, Pro-15 to Gly-21, Gly-54 to Ser-59, Trp-73 to Lys-78, Ser-90 to Arg-104.
694991	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 483 as residues: Lys-1 to Thr-6, Pro-8 to Gly-19, Val-61 to Arg-66.
698669	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 485 as residues: Pro-31 to His-36, Gly-43 to Tyr-48, Glu-136 to Ser-142, Pro-178 to Arg-183, Pro-273 to Asp-278, Gly-318 to Cys-326.
707357	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 488 as residues: Gly-6 to Arg-21, Arg-89 to Asp-94.
707360	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 489 as residues: Ser-13 to Glu-26, Ser-48 to Val-55, Lys-85 to Thr-91, Asp-115 to Trp-120.
707375	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 490 as residues: Arg-1 to Gly-6, Ala-12 to Arg-19, Arg-34 to Arg-40, Arg-47 to Ala-58, Ser-67 to Thr-80, Ser-109 to Ser-117, Asn-134 to Ser-141, Pro-175 to Arg-181, Lys-212 to Thr-218, Asp-275 to Cys-285.
707754	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 491 as residues: Val-32 to Leu-41, Asn-55 to Arg-63, Pro-104 to Ala-113.
712248	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 493 as residues: Ser-13 to Gly-20, Gln-36 to Ser-41, Pro-44 to Phe-58.
715445	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 494 as residues: Gly-23 to Thr-29, Ser-32 to Val-40, Lys-181 to Ser-188, Glu-197 to Gln-204, Arg-244 to His-249, Ala-253 to Thr-264.
716362	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 495 as residues: Cys-1 to Gly-8, Arg-71 to Ser-77, His-102 to Ser-108.
716835	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 496 as residues: Gln-7 to Glu-14, Ala-24 to Arg-41.
717685	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 498 as residues: Gly-1 to Ala-7, His-70 to Gly-76, Gln-130 to Thr-135, Thr-182 to Pro-189, Asn-259 to Leu-267, Glu-280 to Ala-289, Gln-303 to Asn-310.
719755	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 499 as residues: Asp-14 to Pro-25, Pro-59 to Glu-100, Cys-126 to Gly-145, Pro-158 to Lys-164, Lys-176 to Leu-197, Leu-221 to Tyr-238.
720389	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 500 as residues: Thr-13 to Ala-19, Ala-26 to Pro-36, Ser-63 to Gly-68.
720903	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 501 as residues: Asn-6 to Ser-11, Ala-91 to Arg-99, Trp-107 to Tyr-113, Tyr-131 to Met-137, Asp-150 to Val-157.
721562	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 503 as residues: Asp-39 to Ile-45.
722775	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 504 as residues: Pro-34 to Ser-41, Cys-49 to Arg-55, Thr-92 to Ala-98, Thr-160 to Gly-173, Thr-194 to Pro-200, Gly-274 to Trp-282, Pro-285 to Ala-291.
724463	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 505 as residues: Glu-9 to Lys-15, Pro-23 to Tyr-33.
728418	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 507 as residues: Ala-6 to Gln-11, Ser-25 to Ser-30, Lys-63 to Gly-69, Ser-108 to Asp-118, Arg-

	127 to His-132, Asp-156 to Cys-161.
728920	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 508 as residues: Thr-7 to Ala-15.
732958	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 509 as residues: Thr-10 to Ala-15, Pro-63 to Ser-78, Ser-82 to Leu-94.
733134	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 510 as residues: Arg-4 to Gly-24, Lys-47 to Phe-55, Lys-61 to Ala-67, Gly-108 to Thr-114, Pro-184 to Pro-191, Pro-292 to Arg-299, Pro-355 to Glu-392.
734099	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 511 as residues: His-1 to Arg-7, Gln-15 to Ala-23, Met-43 to Gln-55.
738911	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 515 as residues: Arg-4 to Asp-10, Ser-64 to His-75, Pro-127 to Asn-136, Phe-143 to Gln-150.
739226	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 516 as residues: Asn-1 to Thr-7.
739527	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 517 as residues: Gly-1 to Arg-9, Val-28 to Gly-39, Asp-52 to Leu-60, Ala-106 to Trp-117.
744331	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 520 as residues: Ser-17 to Arg-24.
744751	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 521 as residues: Ser-8 to Val-13, Pro-34 to Cys-40, Tyr-48 to Ser-55, Gly-63 to Ser-73.
745750	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 522 as residues: Ser-2 to Glu-17.
746285	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 523 as residues: Lys-87 to Lys-92.
746416	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 524 as residues: Arg-6 to Leu-12, Tyr-18 to Asp-25.
747851	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 525 as residues: Gly-124 to Ser-129, Leu-162 to Gly-167, Val-272 to Ala-278, Lys-293 to Asp-298.
751315	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 527 as residues: Cys-12 to Pro-20.
754634	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 529 as residues: Asp-1 to Thr-10.
756833	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 531 as residues: Thr-36 to Pro-49, Glu-52 to Pro-67.
756878	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 532 as residues: Pro-8 to Lys-15, Gly-69 to Trp-75.
757332	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 533 as residues: Gln-23 to Val-31, Phe-39 to Ile-52.
760835	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 534 as residues: Phe-1 to Lys-7, Cys-82 to Ser-90.
761760	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 535 as residues: Arg-34 to Pro-39, Gly-43 to Asp-51, Gln-147 to Arg-153.
762520	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 536 as residues: His-6 to His-11, Ala-13 to Glu-18, Ala-60 to Ser-65, Ile-72 to Ser-77, Gln-95 to Phe-101, Leu-136 to Ser-142.
764461	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 537 as residues: Val-15 to Ala-22, Val-26 to Gly-38.
764517	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 538 as residues: Gly-30 to Lys-36, Gly-94 to Ala-100, Gln-150 to Gly-156, Gln-189 to Leu-195.
765132	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 539 as residues: Asn-80 to Thr-87, Ser-165 to Leu-182, Thr-196 to His-201, Lys-271 to His-279, Asp-286 to Gly-292, Tyr-294 to Leu-302.
765667	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 540 as residues: Pro-14 to Pro-21, Pro-30 to Pro-36.

767113	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 541 as residues: Ala-62 to Pro-73, Pro-75 to Thr-83, Thr-110 to Phe-115, Glu-142 to Asp-150, Gln-158 to Ser-167, Glu-182 to Thr-187, Ser-190 to Asp-204.
767204	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 542 as residues: Ala-22 to Met-29, Arg-45 to Phe-56, Asp-63 to Asp-71, Gly-81 to Ala-88, Gln-155 to Trp-162.
767962	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 544 as residues: Glu-126 to Gly-132, Asn-146 to Ser-158, Phe-179 to Leu-188.
768040	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 545 as residues: Pro-24 to Trp-32, Val-51 to Arg-62, Gly-84 to Asp-93, Asp-108 to Asn-120, Glu-150 to Val-158, Gly-169 to Gly-175.
769956	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 546 as residues: Pro-1 to Arg-6.
770133	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 547 as residues: Glu-1 to Ser-6.
771964	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 549 as residues: Pro-8 to Gly-15, Thr-26 to Phe-32, Thr-102 to Ser-109, Ala-112 to Thr-118, His-130 to Glu-152, Ser-161 to Ala-170, Ser-204 to His-209, Gly-221 to Ser-229, Ser-233 to Ala-240, Glu-242 to Pro-247, Leu-251 to Gln-258, Leu-278 to Leu-285, Thr-333 to Glu-338.
773387	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 551 as residues: Lys-36 to Lys-45, Ala-59 to Arg-67, Cys-99 to Arg-108, Ala-115 to Cys-125, Arg-143 to Arg-153.
773827	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 552 as residues: Pro-1 to Ala-15, Ser-72 to His-79, Gly-89 to Tyr-105, Lys-179 to Lys-184, Arg-246 to Asp-251, Glu-302 to Lys-309, Ser-329 to Phe-341.
774108	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 553 as residues: Ala-1 to Gly-21, Pro-28 to Leu-39, Pro-48 to Asp-62, Arg-71 to Arg-78.
775339	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 555 as residues: Asp-6 to Thr-13, Asp-24 to Met-30.
775582	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 556 as residues: Gly-1 to Asn-12, Ser-69 to Glu-77.
777809	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 558 as residues: Arg-15 to Gly-25.
778927	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 559 as residues: Ala-74 to Ser-82, Asn-109 to Ala-124, Ser-147 to Ile-152, Pro-188 to Gly-194, Arg-290 to Pro-299, Tyr-307 to Glu-319, Tyr-341 to Ile-346, Lys-423 to Ser-441, Gln-452 to Glu-465.
779262	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 560 as residues: Arg-5 to Ile-24, Gly-35 to Trp-40, Glu-42 to Thr-48, Lys-76 to Gly-95.
780149	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 562 as residues: Gly-13 to Gln-18, Pro-71 to Glu-89, Ile-134 to Asp-139, Pro-232 to Met-240.
780583	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 563 as residues: Asn-58 to Thr-64, Ile-72 to Ser-78, Gly-119 to Lys-128.
780960	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 564 as residues: Ala-7 to Ile-14, Lys-27 to Asp-35, Thr-63 to Leu-73.
781469	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 565 as residues: Pro-1 to Ala-12, Arg-27 to Gln-45, Arg-57 to Gln-64, Lys-74 to Asp-96.
781771	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 567 as residues: Glu-38 to Leu-52, Glu-64 to Lys-72, Asn-92 to Ala-102, Ala-104 to Asp-119, Pro-121 to Pro-130, Ser-165 to Ser-173.
782033	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 568 as residues: Ala-1 to Gly-19, Gln-41 to Gly-46.
782105	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 569 as residues: Leu-13 to Gly-34, Arg-77 to Pro-85, Lys-129 to Arg-135.
782122	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 570 as



	residues: Pro-1 to Arg-6, Ala-102 to Ala-108, Pro-148 to Asp-158, Gly-164 to Ala-171, Pro-223 to Asn-231, Pro-272 to Ser-282, Ala-294 to Pro-310, Pro-322 to Arg-327.
783245	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 572 as residues: Leu-90 to Arg-97, Ala-107 to Pro-113.
783247	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 573 as residues: Ser-2 to Leu-8.
783413	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 574 as residues: Lys-33 to Val-39.
784407	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 575 as residues: Gly-28 to Val-36.
784548	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 576 as residues: Trp-1 to Pro-9, Pro-15 to Gln-24, Pro-52 to Thr-57.
785677	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 578 as residues: Gly-7 to Gly-14.
786238	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 579 as residues: Gly-1 to Gly-8.
786389	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 580 as residues: Ser-2 to Arg-16, Gly-34 to Glu-44, Arg-62 to Gln-69, Pro-102 to Ile-108, Asp-187 to Thr-193, Leu-203 to Pro-213.
786929	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 581 as residues: Pro-2 to Trp-7, Tyr-36 to Tyr-43.
786932	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 582 as residues: Ser-18 to His-30, Thr-39 to Arg-51, Leu-59 to Thr-66, Pro-131 to Lys-136, Pro-149 to Ser-157.
787078	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 583 as residues: Glu-20 to Pro-26.
787283	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 585 as residues: Glu-7 to Arg-13, Gln-26 to Arg-34.
788988	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 587 as residues: Pro-41 to Tyr-50, Thr-70 to Lys-75.
789092	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 588 as residues: Thr-27 to Ala-34, Leu-41 to Glu-48, Glu-76 to Asn-87, Asn-110 to Leu-118, Gly-125 to Lys-133.
789298	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 589 as residues: Arg-1 to Ser-14, Glu-56 to Gly-61, Ala-92 to Gln-98, Glu-134 to Val-154.
789718	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 591 as residues: Cys-17 to Ala-24.
790285	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 594 as residues: Thr-11 to Leu-18, Leu-22 to Val-31, Trp-33 to Lys-49, Ser-63 to Glu-72, Cys-80 to Ala-91, Pro-97 to His-116.
790509	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 595 as residues: Ser-6 to His-20, Leu-22 to Gly-32, Lys-103 to Arg-111, Ser-125 to Gly-130, Glu-204 to His-210, Thr-213 to His-219, Pro-222 to Asp-244, Ser-250 to Glu-258, Arg-263 to Arg-268.
790775	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 596 as residues: Arg-42 to Asp-48, Cys-79 to Thr-85, Leu-113 to Ser-123.
790888	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 597 as residues: Pro-14 to Asp-19, Asp-40 to Leu-45, Ser-53 to Val-58, Leu-81 to Tyr-91.
791506	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 598 as residues: Arg-1 to Gly-9, Asp-19 to His-25, Gly-51 to Glu-61.
792002	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 601 as residues: Arg-1 to Gly-6, Val-22 to Pro-35, Val-106 to Ile-112, His-118 to Gln-124, Ser-132 to Leu-145, Asn-164 to Asn-170, Arg-187 to Tyr-192.
792291	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 602 as residues: Pro-14 to Arg-31.
792371	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 603 as

	residues: Gly-37 to Gly-52, Pro-63 to Gly-69, Ser-74 to His-81, Ser-94 to Thr-105, Val-109 to Thr-114, Phe-165 to Ser-181, Ala-191 to Asp-196, Asn-209 to Ser-216.
792660	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 604 as residues: Thr-11 to Arg-16, Asn-78 to Asp-84.
792782	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 605 as residues: Ala-65 to Gly-81.
792890	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 606 as residues: Pro-26 to His-31, Arg-34 to Ser-44, Pro-59 to Ser-71, Leu-77 to Gly-83.
792931	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 607 as residues: Pro-3 to His-12.
792943	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 608 as residues: Lys-3 to Tyr-9, Gly-15 to Thr-22, Leu-36 to Asp-41, Leu-67 to Lys-76, Asp-86 to Ser-93, Tyr-174 to Asp-184, Leu-255 to Glu-260, Ile-331 to Val-337.
793446	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 611 as residues: His-1 to Gly-12.
793639	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 612 as residues: Arg-6 to Arg-13, Pro-47 to Val-52, Gln-57 to Arg-65, Arg-72 to Glu-78, Asp-117 to Thr-124, Phe-132 to His-137.
794213	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 613 as residues: Tyr-1 to Trp-9, Thr-44 to Leu-49.
795955	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 615 as residues: Lys-60 to Lys-65, Lys-99 to Ala-104.
796555	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 617 as residues: Ser-1 to Gly-10, Glu-90 to Gly-97, Asn-185 to Arg-197, Pro-202 to Arg-211.
796675	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 618 as residues: Ser-35 to Gly-40, Ser-103 to His-109, Tyr-151 to Gly-159, Pro-216 to Glu-224, Asn-249 to Trp-258, Pro-278 to Glu-284.
796743	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 619 as residues: Asn-1 to Gly-6, Asn-100 to Glu-106, Gln-108 to Asp-116, Asp-146 to Thr-151, Thr-191 to Glu-198.
796792	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 620 as residues: Asn-23 to Gly-28, Cys-41 to Asp-47, Gln-82 to Glu-88.
799668	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 621 as residues: Gly-2 to Arg-10, Ile-27 to Pro-33.
799669	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 622 as residues: Gly-1 to Ser-12.
799673	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 623 as residues: Gly-1 to Ala-14, Leu-38 to Pro-46.
799674	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 624 as residues: Pro-39 to Pro-45.
799678	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 625 as residues: Lys-54 to Ser-60, Tyr-86 to His-93.
799728	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 626 as residues: Trp-7 to Gln-19.
799748	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 627 as residues: Glu-7 to Arg-12, Lys-62 to His-68.
799760	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 628 as residues: Ile-15 to Trp-22.
800296	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 630 as residues: Asn-19 to Thr-39, Glu-42 to Ile-48, Arg-55 to Asp-66, Ile-130 to Arg-135, Lys-149 to Ala-156, Glu-166 to Leu-176, Met-213 to Lys-219, Pro-233 to Pro-248, Lys-258 to Lys-263.
800327	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 631 as residues: Arg-13 to Gly-19, Lys-32 to Glu-39, Lys-94 to Trp-100, Asn-102 to Asp-108, Ala-117 to Leu-129.
800816	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 632 as

	residues: Lys-1 to Ile-11, Gln-36 to Leu-46.
800835	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 633 as residues: Trp-1 to Gln-11, Gly-37 to Gln-50, Ser-109 to Gln-114, Glu-146 to Leu-155, Glu-175 to Gly-180, Thr-188 to Ser-200.
805429	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 634 as residues: Pro-6 to Ser-51, Gln-100 to Glu-107.
805458	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 635 as residues: Glu-57 to Ser-62, Thr-102 to Ser-120.
805478	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 636 as residues: Glu-31 to Glu-37, Pro-47 to Ser-52, Asn-57 to Asn-66.
805805	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 637 as residues: Arg-1 to Cys-16, Tyr-59 to Lys-68, Glu-76 to Arg-82.
806486	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 638 as residues: Phe-1 to Val-6, Pro-11 to Gly-18.
806498	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 639 as residues: Pro-6 to Ser-17, Arg-81 to Thr-88, Arg-198 to Val-203, Arg-285 to Arg-296, Gln-302 to Ser-361, Leu-399 to Ser-407.
810870	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 641 as residues: Val-12 to Ile-21.
811730	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 642 as residues: Arg-33 to Arg-40.
813262	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 645 as residues: Gly-31 to Asp-51, Cys-68 to Val-81, Leu-85 to Cys-92.
815637	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 646 as residues: Arg-13 to Asp-19, Ser-80 to Gly-91, Pro-99 to Ser-111.
815853	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 647 as residues: Cys-25 to Ser-31, Gln-63 to Asp-73, Arg-98 to Gly-106, Pro-120 to Arg-125, Leu-136 to Asp-141, Gly-155 to Glu-170, Phe-179 to Gly-186.
815999	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 648 as residues: Asp-1 to Asp-10, Arg-19 to Glu-28, Gly-86 to Leu-93, Arg-113 to His-118.
823427	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 649 as residues: Pro-16 to Cys-27, Arg-70 to Arg-76.
823704	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 650 as residues: Val-29 to Lys-34, Arg-58 to His-63, Gln-87 to Lys-97, Arg-195 to Ser-200.
824798	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 651 as residues: Thr-28 to His-34.
825018	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 652 as residues: Gln-1 to Asn-11, Leu-19 to Thr-24, Lys-47 to Arg-55, Lys-94 to Asp-99, Ala-101 to Arg-107, Ala-137 to Tyr-146, Gln-150 to Ser-163, Gly-169 to Lys-175, Thr-182 to Ala-189, Glu-249 to Ser-258, Pro-266 to Tyr-275, Tyr-285 to Gly-298, Asp-302 to Gln-315, Tyr-318 to Thr-325, Gln-332 to Ala-359, Ser-372 to Phe-384, Leu-390 to Ala-399, Ala-428 to Arg-437.
825787	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 654 as residues: Pro-21 to Leu-28, Arg-40 to Ile-49, Asp-84 to Asn-93, Arg-124 to Asn-130, Gly-140 to Asn-145, Leu-187 to Gln-196, Pro-208 to Asp-213, Arg-244 to Asp-252, Ile-325 to Gln-336, Glu-372 to Ala-379, Asn-435 to Leu-446, Ala-460 to Arg-467, Val-500 to Asp-506, Lys-524 to Asn-533, Thr-592 to Lys-598, Asp-648 to Ser-656.
826116	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 655 as residues: Glu-20 to Cys-35.
826147	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 656 as residues: Lys-18 to Leu-24.
827586	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 658 as residues: Ser-7 to Gly-14, Leu-22 to Ala-28, Thr-57 to Ser-62.
827735	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 660 as residues: Pro-2 to Ser-12, Gln-25 to Glu-31, Val-40 to Arg-45.
827740	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 661 as

	residues: Ile-22 to Lys-28.
827808	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 662 as residues: Glu-2 to Gln-13, Gln-20 to Gly-29, Arg-32 to Cys-47, Pro-54 to Trp-61, Thr-73 to Gln-91, Gly-96 to Ser-103.
828357	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 664 as residues: Gly-1 to Gly-10, Val-25 to Glu-32, His-67 to Arg-73.
828612	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 666 as residues: Asp-25 to Gln-31, Asp-36 to Tyr-41, Gln-43 to Thr-48, Lys-71 to Thr-76.
828647	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 667 as residues: Ser-2 to Ser-8, Arg-61 to Gln-74, Ser-192 to Asn-202, Gln-229 to Lys-236, Gly-281 to Gly-292, Glu-333 to Ala-345, Ala-352 to Gln-358, Glu-360 to Leu-366, Asp-443 to Ser-449, Glu-452 to Glu-459, Asp-485 to Thr-492, Ala-510 to Gln-516, Ala-545 to Ala-552, Leu-560 to Thr-566, Glu-586 to Ala-592, Asp-601 to Gln-607, Leu-609 to Leu-620.
828698	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 668 as residues: Pro-28 to Ser-43, Pro-45 to Ala-50, His-58 to Gln-63.
828962	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 669 as residues: Ala-42 to Gly-49, Thr-54 to Cys-63.
829282	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 671 as residues: Ser-7 to Gln-12, Gly-25 to Gly-31, Gly-71 to Gly-84, Leu-147 to Glu-164, Trp-172 to Leu-180.
829368	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 672 as residues: Glu-1 to Tyr-7, Pro-13 to Glu-24, Arg-31 to Ile-39, Gln-59 to Lys-65, His-67 to Leu-74.
829751	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 673 as residues: Ala-29 to Arg-45, Ser-48 to Glu-59, Lys-73 to Trp-79, Ala-100 to Ser-109.
829934	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 675 as residues: Arg-1 to Arg-6, Ser-46 to Asp-71, Glu-76 to Glu-90, Gln-107 to Tyr-118, Ser-124 to Asp-131, Glu-163 to Asp-170, Ala-239 to Asp-245, Asp-262 to Arg-268, Gln-276 to Asp-283, Arg-293 to Lys-300, Ser-307 to Glu-313, Phe-346 to Phe-351, Phe-361 to Ala-373.
829951	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 677 as residues: Thr-21 to Lys-28.
830173	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 678 as residues: Gly-51 to Asn-68, Thr-75 to Lys-82, Ala-86 to Ala-97, Asn-99 to Arg-106, Leu-121 to Phe-126, Ala-155 to Ser-163, Asp-175 to Asp-180, Ala-184 to Phe-196, Leu-204 to Asn-214, Asp-219 to Gln-232, Leu-269 to Arg-274, Pro-392 to Pro-400, Thr-430 to Asn-437, Tyr-472 to Gln-477, Leu-483 to Gln-499, Asn-516 to Gln-524, Ser-533 to Gln-546, Lys-562 to Glu-576, Leu-589 to Ala-594, Asp-624 to Ala-633, Ile-741 to Asp-746, Val-817 to Lys-839, Tyr-872 to Lys-878, Thr-929 to Asp-940.
830365	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 680 as residues: Trp-36 to Glu-41, Asp-71 to Arg-76, Asn-80 to Gly-87, Arg-103 to Pro-115.
830456	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 681 as residues: Leu-48 to Cys-54.
830549	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 682 as residues: Ser-1 to Pro-24, Pro-40 to Thr-50, Glu-62 to Gly-83, Arg-103 to Leu-108, Ser-141 to Lys-146, Lys-184 to Ser-190.
830602	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 683 as residues: Arg-53 to Thr-63, Ile-100 to Lys-108.
830610	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 684 as residues: Pro-27 to Cys-32, Ala-61 to Gly-70, Pro-76 to Gly-85, Met-115 to Gly-120, Glu-162 to Lys-171, Pro-222 to Tyr-228, Glu-242 to Thr-248, Lys-261 to Gly-269.
830644	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 685 as residues: Ile-1 to Ser-10.
830707	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 686 as residues: Asn-34 to Leu-53, Gln-61 to Leu-67.

830709	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 687 as residues: Arg-13 to Gln-18, Pro-22 to Ala-40, Ala-66 to Asp-84, Glu-94 to Arg-101.
830733	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 688 as residues: Glu-1 to Asp-8.
830855	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 690 as residues: Ser-1 to His-6.
830949	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 691 as residues: Arg-5 to Arg-12, Gly-25 to Trp-30, Thr-77 to Trp-96, Thr-101 to Glu-106, Gly-109 to Arg-127.
830965	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 692 as residues: Leu-24 to Arg-56, Pro-83 to Arg-90, Ile-110 to Ile-115, Lys-123 to Val-136.
830973	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 693 as residues: Ser-1 to Asn-7, Tyr-13 to Asp-23.
830989	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 695 as residues: Cys-2 to Ser-16, Glu-55 to Lys-61, Pro-83 to Leu-88, Ser-135 to Pro-148, Val-152 to Arg-163, Pro-223 to Thr-230, Ala-242 to Val-253, Arg-258 to Glu-274, Gly-290 to Asp-300, Lys-337 to Asn-345, Asp-373 to Ala-398, Gly-401 to Lys-406, Gln-410 to Ala-430, Pro-433 to Gln-460.
831134	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 696 as residues: Ala-19 to His-24.
831200	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 697 as residues: Trp-1 to Gly-6.
831531	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 699 as residues: Ser-94 to Asn-116, Glu-139 to Asp-155, Tyr-190 to Leu-195, Ile-230 to Ile-235, Ser-309 to Glu-317.
831665	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 700 as residues: Leu-4 to Trp-12.
831724	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 701 as residues: Pro-26 to Lys-32.
831884	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 702 as residues: Pro-46 to Ala-52, Thr-68 to Trp-86, Arg-91 to Arg-96, Lys-127 to Asp-141.
831897	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 703 as residues: Pro-10 to Ser-20, Val-73 to Ser-78, Asp-123 to Glu-134, Leu-138 to Val-149, Ala-181 to Ala-187, Thr-189 to Val-196, Arg-213 to Gln-224.
831922	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 704 as residues: Leu-32 to Asp-37, Ile-43 to Asn-49.
832266	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 707 as residues: Ala-73 to Arg-79.
832309	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 708 as residues: Val-10 to Gly-15, Ser-98 to Thr-105.
832342	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 709 as residues: Pro-9 to Trp-16, Thr-66 to Ser-72.
832351	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 710 as residues: Asp-16 to Val-21, Leu-54 to Asp-71.
832352	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 711 as residues: Asp-16 to Val-21, Leu-33 to Asp-50.
832434	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 712 as residues: Tyr-15 to Glu-23, Ser-46 to Arg-51, Gln-56 to Trp-61, Pro-79 to Lys-86.
832490	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 713 as residues: Arg-16 to Gly-23, Ala-37 to Asp-46, Asp-91 to Asp-97.
832573	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 714 as residues: Ala-9 to Gln-16, Glu-21 to Arg-27, Gly-66 to Pro-72.
833394	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 716 as residues: Glu-1 to Gly-6, Asp-12 to Gly-22, Ile-28 to Gln-33, Cys-86 to Gly-92, Gly-96 to Ile-105.
835355	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 717 as

	residues: Glu-8 to Ser-15, Gly-42 to Leu-49, Pro-73 to Gly-79, Tyr-82 to Arg-87, Ser-109 to Gly-118, Glu-122 to Ile-128, Asp-132 to Gly-137, Asp-146 to Arg-151, Pro-153 to Lys-158, Gly-191 to His-197, Tyr-210 to Ser-218, Lys-234 to Gly-239, Ala-246 to Ala-252, His-257 to Pro-268, Ser-274 to Gly-280, Pro-316 to Tyr-323, Ile-358 to Leu-363, Gln-375 to Tyr-381, Gln-390 to Tyr-397, Gln-418 to Cys-430.
835497	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 718 as residues: Glu-141 to Pro-151, Asp-179 to Glu-184, Gly-214 to Ser-219, Thr-226 to Tyr-231, Thr-239 to Gly-248, Pro-281 to Gly-297, Pro-326 to Arg-336, Gln-408 to Asp-416.
835978	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 720 as residues: Trp-25 to Val-31.
836274	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 722 as residues: Ser-1 to Glu-9.
836731	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 723 as residues: Lys-15 to Glu-22, Gly-25 to Ala-34, Glu-75 to Gly-81, Gln-91 to Val-100, Pro-146 to Glu-155, Gln-161 to Phe-167, Asn-170 to Gly-178.
838014	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 724 as residues: Arg-1 to Pro-10, Asp-170 to Pro-176, Arg-203 to Tyr-212, Gly-228 to Lys-235.
838874	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 725 as residues: Gln-30 to Gln-45.
839120	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 726 as residues: Thr-22 to Arg-27, Arg-69 to Gly-75, Leu-77 to Pro-85.
839611	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 727 as residues: Asp-12 to Thr-17.
840138	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 728 as residues: Ser-1 to Thr-10.
840616	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 729 as residues: Lys-93 to Gly-99, Glu-144 to Leu-160, Ser-265 to Asp-270, Thr-382 to Gln-396, Val-512 to Val-517, Glu-519 to Asp-535.
840780	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 730 as residues: Leu-8 to Gly-14, Pro-151 to Glu-157.
840857	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 731 as residues: Gln-7 to Glu-22, Ala-27 to Arg-46, Ser-138 to Lys-147, Lys-158 to Pro-163, Asn-171 to Glu-187, Glu-202 to Val-208, Glu-234 to Gly-240, Ser-253 to Lys-260, Gln-272 to Pro-279, Arg-292 to Glu-307, Arg-310 to Arg-317, Asp-342 to Gly-351, Pro-367 to Gly-375, Pro-378 to Arg-388, Leu-425 to Ala-447, Arg-536 to Asp-544, Lys-551 to Lys-561, Val-599 to Asp-604, Ser-622 to Ala-630, Pro-653 to Phe-659, Thr-666 to Ile-673, Pro-699 to Phe-705, Asn-709 to Gly-719, Ala-725 to Phe-737.
840862	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 732 as residues: Arg-2 to Pro-12, Lys-32 to Asn-37, His-75 to Asn-82.
840864	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 733 as residues: Pro-17 to Arg-30, Cys-34 to Gly-40, Met-74 to Glu-81, Pro-106 to Asp-111, Val-136 to Cys-147, Asn-192 to Asp-198.
840938	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 735 as residues: Ser-140 to Thr-148, Thr-194 to Lys-202.
841884	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 736 as residues: Thr-34 to Glu-47.
842241	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 737 as residues: Thr-92 to Lys-101, Glu-134 to Thr-142, Glu-149 to Lys-155, Trp-179 to Ser-187, Thr-205 to Arg-211, Ser-218 to Tyr-225, Asp-283 to Gln-290, Glu-292 to Ile-302, Asn-304 to Met-315.
843712	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 738 as residues: Arg-10 to Asn-16, Ala-59 to Pro-67.
844040	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 739 as residues: Phe-59 to Glu-68, Lys-105 to Gly-111.
844617	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 742 as

	residues: Arg-1 to Lys-7.
846187	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 745 as residues: Gly-8 to Gly-14, Gly-41 to Glu-48, Glu-54 to Lys-74, Glu-87 to Arg-98, Thr-158 to Asn-166, Gly-247 to Ser-254, Gly-257 to Arg-277, Ala-437 to Ser-444, Lys-505 to Arg-510, Phe-519 to Tyr-525, Lys-531 to Pro-538, Gly-562 to Leu-571, Phe-606 to Val-613, Val-692 to Ala-697, Ser-705 to Leu-715, Leu-742 to Cys-747.
HANGA53R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 749 as residues: Arg-4 to Ser-9.
HAHCP93R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 752 as residues: Ser-1 to Ser-12, Thr-23 to Arg-28.
HBGAA76R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 753 as residues: Ser-4 to Ser-11, Pro-27 to Asn-37.
HTXPI29R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 756 as residues: Thr-17 to Leu-24, Thr-57 to Tyr-67, Leu-92 to Phe-102, Asn-128 to Gln-134.
HBGAA54R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 760 as residues: Arg-62 to Leu-70, Ile-74 to Arg-79.
HDPJR77R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 763 as residues: Glu-7 to Lys-22, Thr-33 to Glu-39, Lys-69 to Glu-76, Asp-84 to Tyr-90.
HTTIO41R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 764 as residues: Val-17 to Ser-22, Arg-41 to Glu-46, Lys-50 to Pro-75, Ser-92 to Pro-100.
HDPUL86R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 767 as residues: Lys-7 to Gly-13.
HTXNT16R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 768 as residues: Leu-67 to Asn-72, Thr-102 to Phe-111, Gly-127 to Gln-135.
HLXNA54R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 770 as residues: Gln-1 to Glu-6, Pro-23 to Trp-31, Arg-46 to Trp-51.
H2LAX93R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 772 as residues: Glu-3 to Gln-10.
HWAFW10R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 773 as residues: Glu-13 to Asp-22, His-34 to Trp-40, Arg-69 to Lys-75.
HBGDD17R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 775 as residues: Arg-23 to Thr-28, Pro-40 to Glu-51, Ala-62 to His-68.
H2CBB43R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 778 as residues: Asp-90 to Asp-95, Arg-106 to Thr-117.
H2CBQ77R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 779 as residues: Asp-11 to Gly-16, Gln-19 to Tyr-24, Pro-34 to Gly-46.
HOEMK06R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 781 as residues: Pro-1 to Gln-14.
HCHAG30R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 783 as residues: Gly-1 to Trp-7.
HAEAI26R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 788 as residues: Lys-32 to Val-40, Arg-43 to Pro-51.
H2CBN76R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 791 as residues: Ala-17 to Leu-22, Thr-72 to Lys-77.
HAGFX49R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 792 as residues: Ala-10 to Leu-15, His-64 to Cys-71.
HTXKR32R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 794 as residues: Ser-2 to Gly-12, Glu-57 to Val-65.
H6EAF46R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 796 as residues: Arg-11 to Ser-21.
H2LAK40R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 798 as residues: Glu-11 to Lys-20, Pro-22 to Arg-28.
H2LAY71R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 799 as residues: Arg-26 to Leu-36, Gln-82 to Asp-101, Arg-103 to Arg-108, Arg-113 to Arg-131.
HASAW80R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 803 as

	residues: Gly-1 to Arg-6, Ala-19 to Pro-27, Gly-34 to Phe-40.
HCHAF25R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 804 as residues: Ser-30 to Thr-40, Leu-78 to Val-85, Asp-92 to Ala-97.
HLTHH84R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 805 as residues: Glu-2 to Ala-8.
HADDC09R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 808 as residues: Leu-3 to Gly-9, Thr-20 to Gly-29.
HAQA110R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 811 as residues: Gly-1 to Lys-21.
HBGBT78R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 814 as residues: Asn-1 to Lys-22.
HBGCB06R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 815 as residues: Phe-1 to Phe-15.
HCHMW05R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 823 as residues: Pro-6 to Ser-11.
HODFW25R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 829 as residues: Ser-1 to Thr-8, Glu-17 to Ala-32, Arg-39 to Trp-47.
HOEMQ91R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 830 as residues: Arg-8 to Ser-13.
HOBG56R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 831 as residues: Lys-20 to Arg-25.



The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of the polypeptide sequence shown in SEQ ID NO:Y, or an epitope of the polypeptide sequence encoded by the cDNA in the related cDNA clone contained in a deposited library or encoded by a polynucleotide that hybridizes to the complement of an epitope encoding sequence of SEQ ID NO:X, or an epitope encoding sequence contained in  
5 the deposited cDNA clone under stringent hybridization conditions, or alternatively, under lower stringency hybridization conditions, as defined supra. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X), polynucleotide  
10 sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to this complementary strand under stringent hybridization conditions or alternatively, under lower stringency hybridization conditions, as defined supra.

The term "epitopes," as used herein, refers to portions of a polypeptide having  
15 antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example,  
20 by the methods for generating antibodies described infra. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but  
25 does not necessarily exclude cross- reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

30 In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at

least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., *Cell* 37:767-778 (1984); Sutcliffe et al., *Science* 219:660-666 (1983)).

Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., *supra*; Wilson et al., *supra*; Chow et al., *Proc. Natl. Acad. Sci. USA* 82:910-914; and Bittle et al., *J. Gen. Virol.* 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, in vivo immunization, in vitro immunization, and phage display methods. See, e.g., Sutcliffe et al., *supra*; Wilson et al., *supra*, and Bittle et al., *J. Gen. Virol.*, 66:2347-2354 (1985). If in vivo immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice

are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 µg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention, and immunogenic and/or antigenic epitope fragments thereof can be fused to other polypeptide sequences. For example, the polypeptides of the present invention may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof) resulting in chimeric polypeptides. Such fusion proteins may facilitate purification and may increase half-life in vivo. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., *Nature*, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG Fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion disulfide bonds have also been found to be more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., *J. Biochem.*, 270:3958-3964 (1995).

Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, may be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for

immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D. Bennett et al., *J. Molecular Recognition* 8:52-58 (1995); K. Johanson et al., *J. Biol. Chem.* 270:9459-9471 (1995).)

5        Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., *Proc. Natl. Acad. Sci. USA* 86:821-824 (1989), for instance, hexa-histidine provides for  
10        convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., *Cell* 37:767 (1984).)

      Thus, any of these above fusions can be engineered using the polynucleotides or the  
15        polypeptides of the present invention.

      Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin ("HA") tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed  
20        in human cell lines (Janknecht et al., *Proc. Natl. Acad. Sci. USA* 88:8972- 897 (1991)). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto  
25        Ni<sup>2+</sup> nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

      Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to modulate the activities  
30        of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al.,

Curr. Opin. Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308- 13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of polynucleotides corresponding to SEQ ID NO:X and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments by homologous or site-specific recombination to generate variation in the polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

As discussed herein, any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, polypeptides of the present invention which are shown to be secreted can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

In certain preferred embodiments, proteins of the invention comprise fusion proteins wherein the polypeptides are N and/or C- terminal deletion mutants. In preferred embodiments, the application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to the nucleic acid sequences encoding polypeptides having the amino acid sequence of the specific N- and C-terminal deletions mutants. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

#### 10 **Vectors, Host Cells, and Protein Production**

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides of the invention may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples of appropriate hosts include,

but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells (e.g., *Saccharomyces cerevisiae* or *Pichia pastoris* (ATCC Accession No. 201178)); insect cells such as *Drosophila* S2 and *Spodoptera Sf9* cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells.

5 Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-  
10 3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1,  
15 pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlsbad, CA). Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in  
20 many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid  
25 extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention can also be recovered from: products purified  
30 from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast,

higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

In one embodiment, the yeast *Pichia pastoris* is used to express polypeptides of the invention in a eukaryotic system. *Pichia pastoris* is a methylotrophic yeast which can metabolize methanol as its sole carbon source. A main step in the methanol metabolism pathway is the oxidation of methanol to formaldehyde using O<sub>2</sub>. This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, *Pichia pastoris* must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O<sub>2</sub>. Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (*AOX1*) is highly active. In the presence of methanol, alcohol oxidase produced from the *AOX1* gene comprises up to approximately 30% of the total soluble protein in *Pichia pastoris*. See, Ellis, S.B., et al., *Mol. Cell. Biol.* 5:1111-21 (1985); Koutz, P.J., et al., *Yeast* 5:167-77 (1989); Tschopp, J.F., et al., *Nucl. Acids Res.* 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the *AOX1* regulatory sequence is expressed at exceptionally high levels in *Pichia* yeast grown in the presence of methanol.

In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "*Pichia* Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector allows expression and secretion of a polypeptide of the invention by virtue of the strong *AOX1* promoter linked to



the *Pichia pastoris* alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYDI, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as long as the proposed expression construct provides appropriately located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983, Proteins: Structures and Molecular Principles, W.H. Freeman & Co., N.Y., and Hunkapiller et al., Nature, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide can be synthesized by use of a peptide synthesizer. Furthermore, if desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the

polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid,  $\alpha$ -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoro-amino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

Non-naturally occurring variants may be produced using art-known mutagenesis techniques, which include, but are not limited to oligonucleotide mediated mutagenesis, alanine scanning, PCR mutagenesis, site directed mutagenesis (*see, e.g., Carter et al., Nucl. Acids Res. 13:4331 (1986); and Zoller et al., Nucl. Acids Res. 10:6487 (1982)*), cassette mutagenesis (*see, e.g., Wells et al., Gene 34:315 (1985)*), restriction selection mutagenesis (*see, e.g., Wells et al., Philos. Trans. R. Soc. London SerA 317:415 (1986)*).

The invention additionally, encompasses polypeptides of the present invention which are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease,  $\text{NaBH}_4$ ; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased

solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example, the polyethylene glycol may have an average molecular weight of about 200; 500; 1000; 1500; 2000; 2500; 3000; 3500; 4000; 4500; 5000; 5500; 6000; 6500; 7000; 7500; 8000; 8500; 9000; 9500; 10,000; 10,500; 11,000; 11,500; 12,000; 12,500; 13,000; 13,500; 14,000; 14,500; 15,000; 15,500; 16,000; 16,500; 17,000; 17,500; 18,000; 18,500; 19,000; 19,500; 20,000; 25,000; 30,000; 35,000; 40,000; 50,000; 55,000; 60,000; 65,000; 70,000; 75,000; 80,000; 85,000; 90,000; 95,000; or 100,000 kDa.

As noted above, the polyethylene glycol may have a branched structure. Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo *et al.*, *Appl. Biochem. Biotechnol.* 56:59-72 (1996); Vorobjev *et al.*, *Nucleosides Nucleotides* 18:2745-2750 (1999); and Caliceti *et al.*, *Bioconjug. Chem.* 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, e.g., EP 0 401 384, herein incorporated by reference (coupling PEG to G-CSF), see also Malik *et al.*, *Exp. Hematol.* 20:1028-1035 (1992) (reporting pegylation of GM-CSF using tresyl chloride). For example, polyethylene glycol may be covalently bound through amino acid residues via a

reactive group, such as, a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid residues and the C-terminal amino acid residue. Sulphydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be attached to the protein either directly or by an intervening linker. Linkerless systems for attaching polyethylene glycol to proteins are described in Delgado *et al.*, *Crit. Rev. Thera. Drug Carrier Sys.* 9:249-

304 (1992); Francis *et al.*, *Intern. J. of Hematol.* 68:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated herein by reference.

One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride ( $\text{ClSO}_2\text{CH}_2\text{CF}_3$ ). Upon reaction of protein with tresylated MPEG, polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoroethane sulphonyl group.

Polyethylene glycol can also be attached to proteins using a number of different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number additional polyethylene glycol derivatives and reaction chemistries for attaching polyethylene glycol to proteins are described in WO 98/32466, the entire disclosure of which is incorporated herein by reference. Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

The number of polyethylene glycol moieties attached to each protein of the invention (*i.e.*, the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of substitution within ranges such as 1-3, 2-4, 3-5, 4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado *et al.*, *Crit. Rev. Thera. Drug Carrier Sys.* 9:249-304 (1992).

The breast/ovarian cancer antigen polypeptides of the invention may be in monomers or multimers (*i.e.*, dimers, trimers, tetramers and higher multimers). Accordingly, the present

invention relates to monomers and multimers of the polypeptides of the invention, their preparation, and compositions (preferably, Therapeutics) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers,  
5 or at least tetramers.

Multimers encompassed by the invention may be homomers or heteromers. As used herein, the term homomer, refers to a multimer containing only polypeptides corresponding to the amino acid sequence of SEQ ID NO:Y or an amino acid sequence encoded by SEQ ID NO:X, and/or an amino acid sequence encoded by the cDNA in a related cDNA clone  
10 contained in a deposited library (including fragments, variants, splice variants, and fusion proteins, corresponding to any one of these as described herein). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid sequence. In another specific embodiment, a homomer of the  
15 invention is a multimer containing polypeptides having different amino acid sequences. In specific embodiments, the multimer of the invention is a homodimer (e.g., containing polypeptides having identical or different amino acid sequences) or a homotrimer (e.g., containing polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at  
20 least a homotrimer, or at least a homotetramer.

As used herein, the term heteromer refers to a multimer containing one or more heterologous polypeptides (i.e., polypeptides of different proteins) in addition to the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric  
25 multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked, by for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example,  
30 homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or heterotetramers, are formed when polypeptides of the invention

contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence (e.g., that recited in SEQ ID NO:Y, or contained in a polypeptide encoded by SEQ ID NO:X, and/or by the cDNA in the related cDNA clone contained in a deposited library). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a fusion protein. In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., US Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from another protein that is capable of forming covalently associated multimers, such as for example, oseteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., Science 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the

invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.

Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (FEBS Letters 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.

In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention containing Flag® polypeptide sequence. In a further embodiment, associations proteins of the invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely modified by the addition of cysteine or biotin to the C-terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the polypeptide



components desired to be contained in the multimer of the invention (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the invention to a sequence encoding a linker polypeptide and then further to a synthetic polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hydrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

### Antibodies

Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of SEQ ID NO:Y, and/or an epitope, of the present invention (as determined by immunoassays well known in the art for assaying specific antibody-antigen binding). Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG,

IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule.

Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')<sub>2</sub>, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, ship rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, or by size in contiguous amino acid residues. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that

specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog, or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or  $K_d$  less than  $5 \times 10^{-2}$  M,  $10^{-2}$  M,  $5 \times 10^{-3}$  M,  $10^{-3}$  M,  $5 \times 10^{-4}$  M,  $10^{-4}$  M,  $5 \times 10^{-5}$  M,  $10^{-5}$  M,  $5 \times 10^{-6}$  M,  $10^{-6}$  M,  $5 \times 10^{-7}$  M,  $10^{-7}$  M,  $5 \times 10^{-8}$  M,  $10^{-8}$  M,  $5 \times 10^{-9}$  M,  $10^{-9}$  M,  $5 \times 10^{-10}$  M,  $10^{-10}$  M,  $5 \times 10^{-11}$  M,  $10^{-11}$  M,  $5 \times 10^{-12}$  M,  $10^{-12}$  M,  $5 \times 10^{-13}$  M,  $10^{-13}$  M,  $5 \times 10^{-14}$  M,  $10^{-14}$  M,  $5 \times 10^{-15}$  M, or  $10^{-15}$  M.

The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein. In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85 %, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50%.

Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described supra). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., *Blood* 92(6):1981-1988 (1998); Chen et al., *Cancer Res.* 58(16):3668-3678 (1998); Harrop et al., *J. Immunol.* 161(4):1786-1794 (1998); Zhu et al., *Cancer Res.* 58(15):3209-3214 (1998); Yoon et al., *J. Immunol.* 160(7):3170-3179 (1998); Prat et al., *J. Cell. Sci.* 111(Pt2):237-247 (1998); Pitard et al., *J. Immunol. Methods* 205(2):177-190 (1997); Liautard et al., *Cytokine* 9(4):233-241 (1997); Carlson et al., *J. Biol.*

Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

Antibodies of the present invention may be used, for example, but not limited to, to  
5 purify, detect, and target the polypeptides of the present invention, including both in vitro and in vivo diagnostic and therapeutic methods. For example, the antibodies have use in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988) (incorporated by reference  
10 herein in its entirety).

As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalently and non-covalently conjugations) to polypeptides or other  
15 compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387.

The antibodies of the invention include derivatives that are modified, i.e., by the  
20 covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other  
25 protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

The antibodies of the present invention may be generated by any suitable method  
30 known in the art. Polyclonal antibodies to an antigen-of-interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to

induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples. In a non-limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by

fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')<sub>2</sub> fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')<sub>2</sub> fragments). F(ab')<sub>2</sub> fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain.

For example, the antibodies of the present invention can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., *J. Immunol. Methods* 182:41-50 (1995); Ames et al., *J. Immunol. Methods* 184:177-186 (1995); Kettleborough et al., *Eur. J. Immunol.* 24:952-958 (1994); Persic et al., *Gene* 187 9-18 (1997); Burton et al., *Advances in Immunology* 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any

desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')<sub>2</sub> fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., *BioTechniques* 12(6):864-869 (1992); and Sawai et al., *AJRI* 34:26-34 (1995); and Better et al., *Science* 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., *Methods in Enzymology* 203:46-88 (1991); Shu et al., *PNAS* 90:7995-7999 (1993); and Skerra et al., *Science* 240:1038-1040 (1988). For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, *Science* 229:1202 (1985); Oi et al., *BioTechniques* 4:214 (1986); Gillies et al., (1989) *J. Immunol. Methods* 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., *Nature* 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, *Molecular Immunology* 28(4/5):489-498 (1991); Studnicka et al., *Protein*



Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, Int. Rev. Immunol. 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent

No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed  
5 against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., Bio/technology 12:899-903  
10 (1988)).

Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotypic antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, FASEB J. 7(5):437-444; (1989) and Nissinoff, J. Immunol. 147(8):2429-2438 (1991)). For example, antibodies  
15 which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand. For  
20 example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligands/receptors, and thereby block its biological activity.

#### ***Polynucleotides Encoding Antibodies***

The invention further provides polynucleotides comprising a nucleotide sequence  
25 encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or alternatively, under lower stringency hybridization conditions, e.g., as defined supra, to polynucleotides that encode an antibody, preferably, that specifically binds to a polypeptide of the invention, preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y.

30 The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody may be

assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., *BioTechniques* 17:242 (1994)), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence and corresponding amino acid sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, *Molecular Cloning, A Laboratory Manual*, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel et al., eds., 1998, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties ), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well known in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework

regions to humanize a non-human antibody, as described supra. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed supra, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described supra, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423-42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in E. coli may also be used (Skerra et al., Science 242:1038-1041 (1988)).

#### ***Methods of Producing Antibodies***

The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein.

Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention in situ. These include but are not

limited to microorganisms such as bacteria (e.g., *E. coli*, *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., *Saccharomyces*, *Pichia*) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell  
5 systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3 cells) harboring  
10 recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as *Escherichia coli*, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant  
15 antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., *Gene* 45:101 (1986); Cockett et al., *Bio/Technology* 8:2 (1990)).

In bacterial systems, a number of expression vectors may be advantageously selected  
20 depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the *E. coli* expression vector pUR278 (Ruther et al.,  
25 *EMBO J.* 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, *Nucleic Acids Res.* 13:3101-3109 (1985); Van Heeke & Schuster, *J. Biol. Chem.* 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase  
30 (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or

factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells.

5 The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

In mammalian host cells, a number of viral-based expression systems may be utilized.

10 In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & 15 Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can 20 be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion 25 desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, 30 eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS,

MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed in tk-, hgp<sup>r</sup>t- or ap<sup>r</sup>t- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 Clinical Pharmacy 12:488-505; Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, 1993, TIB TECH 11(5):155-215; and hyg<sup>r</sup>, which confers resistance to hygromycin (Santerre et al., Gene 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.),



Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin et al., J. Mol. Biol. 150:1 (1981), which are incorporated by  
5 reference herein in their entireties.

The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing  
10 antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., Mol. Cell. Biol. 3:257 (1983)).

The host cell may be co-transfected with two expression vectors of the invention, the  
15 first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to  
20 avoid an excess of toxic free heavy chain (Proudfoot, Nature 322:52 (1986); Kohler, Proc. Natl. Acad. Sci. USA 77:2197 (1980)). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

Once an antibody molecule of the invention has been produced by an animal, chemically synthesized, or recombinantly expressed, it may be purified by any method  
25 known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. In addition, the antibodies of the present invention or fragments thereof can be fused to heterologous polypeptide  
30 sequences described herein or otherwise known in the art, to facilitate purification.

The present invention encompasses antibodies recombinantly fused or chemically conjugated (including both covalently and non-covalently conjugations) to a polypeptide (or

portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. The antibodies may be specific for antigens other than polypeptides (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention. For example, antibodies may be used to target the polypeptides of the present invention to particular cell types, either in vitro or in vivo, by fusing or conjugating the polypeptides of the present invention to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to the polypeptides of the present invention may also be used in in vitro immunoassays and purification methods using methods known in the art. See e.g., Harbor et al., supra, and PCT publication WO 93/21232; EP 439,095; Naramura et al., Immunol. Lett. 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., PNAS 89:1428-1432 (1992); Fell et al., J. Immunol. 146:2446-2452(1991), which are incorporated by reference in their entireties.

The present invention further includes compositions comprising the polypeptides of the present invention fused or conjugated to antibody domains other than the variable regions. For example, the polypeptides of the present invention may be fused or conjugated to an antibody Fc region, or portion thereof. The antibody portion fused to a polypeptide of the present invention may comprise the constant region, hinge region, CH1 domain, CH2 domain, and CH3 domain or any combination of whole domains or portions thereof. The polypeptides may also be fused or conjugated to the above antibody portions to form multimers. For example, Fc portions fused to the polypeptides of the present invention can form dimers through disulfide bonding between the Fc portions. Higher multimeric forms can be made by fusing the polypeptides to portions of IgA and IgM. Methods for fusing or conjugating the polypeptides of the present invention to antibody portions are known in the art. See, e.g., U.S. Patent Nos. 5,336,603; 5,622,929; 5,359,046; 5,349,053; 5,447,851; 5,112,946; EP 307,434; EP 367,166; PCT publications WO 96/04388; WO 91/06570; Ashkenazi et al., Proc. Natl. Acad. Sci. USA 88:10535-10539 (1991); Zheng et al., J. Immunol. 154:5590-5600 (1995); and Vil et al., Proc. Natl. Acad. Sci. USA 89:11337-11341(1992) (said references incorporated by reference in their entireties).

As discussed, supra, the polypeptides corresponding to a polypeptide, polypeptide fragment, or a variant of SEQ ID NO:Y may be fused or conjugated to the above antibody portions to increase the in vivo half life of the polypeptides or for use in immunoassays using

methods known in the art. Further, the polypeptides corresponding to SEQ ID NO:Y may be fused or conjugated to the above antibody portions to facilitate purification. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP 394,827; Traunecker et al., *Nature* 331:84-86 (1988)). The polypeptides of the present invention fused or conjugated to an antibody having disulfide-linked dimeric structures (due to the IgG) may also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., *J. Biochem.* 270:3958-3964 (1995)). In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP A 232,262). Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, Bennett et al., *J. Molecular Recognition* 8:52-58 (1995); Johanson et al., *J. Biol. Chem.* 270:9459-9471 (1995)).

Moreover, the antibodies or fragments thereof of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., *Proc. Natl. Acad. Sci. USA* 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the "HA" tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., *Cell* 37:767 (1984)) and the "flag" tag.

The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent

materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Patent No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{111}\text{In}$  or  $^{99}\text{Tc}$ .

Further, an antibody or fragment thereof may be conjugated to a therapeutic moiety such as a cytotoxin, e.g., a cytostatic or cytotoxic agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example,  $^{213}\text{Bi}$ . A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis- dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

The conjugates of the invention can be used for modifying a given biological response, the therapeutic agent or drug moiety is not to be construed as limited to classical

chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor,  $\alpha$ -interferon,  $\beta$ -interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, e.g., TNF- $\alpha$ , TNF- $\beta$ , AIM I (See, 5 International Publication No. WO 97/33899), AIM II (See, International Publication No. WO 97/34911), Fas Ligand (Takahashi *et al.*, *Int. Immunol.*, 6:1567-1574 (1994)), VEGI (See, International Publication No. WO 99/23105), a thrombotic agent or an anti-angiogenic agent, e.g., angiostatin or endostatin; or, biological response modifiers such as, for example, 10 lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not 15 limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Techniques for conjugating such therapeutic moiety to antibodies are well known, see, e.g., Arnon *et al.*, "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in *Monoclonal Antibodies And Cancer Therapy*, Reisfeld *et al.* (eds.), pp. 243-56 20 (Alan R. Liss, Inc. 1985); Hellstrom *et al.*, "Antibodies For Drug Delivery", in *Controlled Drug Delivery* (2nd Ed.), Robinson *et al.* (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera *et al.* (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of 25 Radiolabeled Antibody In Cancer Therapy", in *Monoclonal Antibodies For Cancer Detection And Therapy*, Baldwin *et al.* (eds.), pp. 303-16 (Academic Press 1985), and Thorpe *et al.*, "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", *Immunol. Rev.* 62:119-58 (1982).

Alternatively, an antibody can be conjugated to a second antibody to form an 30 antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

An antibody, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

## 5 *Immunophenotyping*

The antibodies of the invention may be utilized for immunophenotyping of cell lines and biological samples. The translation product of the gene of the present invention may be useful as a cell specific marker, or more specifically as a cellular marker that is differentially expressed at various stages of differentiation and/or maturation of particular cell types.

10 Monoclonal antibodies directed against a specific epitope, or combination of epitopes, will allow for the screening of cellular populations expressing the marker. Various techniques can be utilized using monoclonal antibodies to screen for cellular populations expressing the marker(s), and include magnetic separation using antibody-coated magnetic beads, "panning" with antibody attached to a solid matrix (i.e., plate), and flow cytometry (See, e.g., U.S. Patent 5,985,660; and Morrison *et al.*, *Cell*, 96:737-49 (1999)).

15 These techniques allow for the screening of particular populations of cells, such as might be found with hematological malignancies (i.e. minimal residual disease (MRD) in acute leukemic patients) and "non-self" cells in transplantations to prevent Graft-versus-Host Disease (GVHD). Alternatively, these techniques allow for the screening of hematopoietic stem and progenitor cells capable of undergoing proliferation and/or differentiation, as might be found in human umbilical cord blood.

## *Assays For Antibody Binding*

25 The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, 30 immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York,

which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

Immunoprecipitation protocols generally comprise lysing a population of cells in a lysis buffer such as RIPA buffer (1% NP-40 or Triton X-100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 0.01 M sodium phosphate at pH 7.2, 1% Trasylol) supplemented with protein phosphatase and/or protease inhibitors (e.g., EDTA, PMSF, aprotinin, sodium vanadate), adding the antibody of interest to the cell lysate, incubating for a period of time (e.g., 1-4 hours) at 4° C, adding protein A and/or protein G sepharose beads to the cell lysate, incubating for about an hour or more at 4° C, washing the beads in lysis buffer and resuspending the beads in SDS/sample buffer. The ability of the antibody of interest to immunoprecipitate a particular antigen can be assessed by, e.g., western blot analysis. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the binding of the antibody to an antigen and decrease the background (e.g., pre-clearing the cell lysate with sepharose beads). For further discussion regarding immunoprecipitation protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.16.1.

Western blot analysis generally comprises preparing protein samples, electrophoresis of the protein samples in a polyacrylamide gel (e.g., 8%-20% SDS-PAGE depending on the molecular weight of the antigen), transferring the protein sample from the polyacrylamide gel to a membrane such as nitrocellulose, PVDF or nylon, blocking the membrane in blocking solution (e.g., PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (e.g., PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, e.g., an anti-human antibody) conjugated to an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) or radioactive molecule (e.g., <sup>32</sup>P or <sup>125</sup>I) diluted in blocking buffer, washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.8.1.

ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the art. For further discussion regarding ELISAs see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 11.2.1.

The binding affinity of an antibody to an antigen and the off-rate of an antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (e.g.,  $^3\text{H}$  or  $^{125}\text{I}$ ) with the antibody of interest in the presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of interest for a particular antigen and the binding off-rates can be determined from the data by scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays. In this case, the antigen is incubated with antibody of interest conjugated to a labeled compound (e.g.,  $^3\text{H}$  or  $^{125}\text{I}$ ) in the presence of increasing amounts of an unlabeled second antibody.

## 25 *Therapeutic Uses*

The present invention is further directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the disclosed diseases, disorders, or conditions. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of



the invention can be used to treat, inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions described herein. The treatment and/or prevention of diseases, disorders, or conditions associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, e.g., IL-2, IL-3 and IL-7), for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

The antibodies of the invention may be administered alone or in combination with other types of treatments (e.g., radiation therapy, chemotherapy, hormonal therapy, immunotherapy and anti-tumor agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides of the invention, including fragments thereof. Preferred binding affinities

include those with a dissociation constant or  $K_d$  less than  $5 \times 10^{-2}$  M,  $10^{-2}$  M,  $5 \times 10^{-3}$  M,  $10^{-3}$  M,  $5 \times 10^{-4}$  M,  $10^{-4}$  M,  $5 \times 10^{-5}$  M,  $10^{-5}$  M,  $5 \times 10^{-6}$  M,  $10^{-6}$  M,  $5 \times 10^{-7}$  M,  $10^{-7}$  M,  $5 \times 10^{-8}$  M,  $10^{-8}$  M,  $5 \times 10^{-9}$  M,  $10^{-9}$  M,  $5 \times 10^{-10}$  M,  $10^{-10}$  M,  $5 \times 10^{-11}$  M,  $10^{-11}$  M,  $5 \times 10^{-12}$  M,  $10^{-12}$  M,  $5 \times 10^{-13}$  M,  $10^{-13}$  M,  $5 \times 10^{-14}$  M,  $10^{-14}$  M,  $5 \times 10^{-15}$  M, and  $10^{-15}$  M.

5

### *Gene Therapy*

In a specific embodiment, nucleic acids comprising sequences encoding antibodies or functional derivatives thereof, are administered to treat, inhibit or prevent a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., *Clinical Pharmacy* 12:488-505 (1993); Wu and Wu, *Biotherapy* 3:87-95 (1991); Tolstoshev, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596 (1993); Mulligan, *Science* 260:926-932 (1993); and Morgan and Anderson, *Ann. Rev. Biochem.* 62:191-217 (1993); May, *TIBTECH* 11(5):155-215 (1993). Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, NY (1993); and Kriegler, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY (1990).

In a preferred aspect, the compound comprises nucleic acid sequences encoding an antibody, said nucleic acid sequences being part of expression vectors that express the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment, nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody encoding nucleic acids (Koller and Smithies, *Proc. Natl. Acad. Sci. USA* 86:8932-8935 (1989); Zijlstra et al., *Nature* 342:435-438 (1989).

In specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.

Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid- carrying vectors, or indirect, in which case, cells are first transformed with the nucleic acids in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid sequences are directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)).

In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention are used. For example, a retroviral vector can be used (see Miller et al., Meth. Enzymol. 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the

host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., *Biotherapy* 6:291-302 (1994), which describes the use of a retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., *J. Clin. Invest.* 93:644-651 (1994); Kiem et al., *Blood* 83:1467-1473 (1994); Salmons and Gunzberg, *Human Gene Therapy* 4:129-141 (1993); and Grossman and Wilson, *Curr. Opin. in Genetics and Devel.* 3:110-114 (1993).

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, *Current Opinion in Genetics and Development* 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., *Human Gene Therapy* 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., *Science* 252:431-434 (1991); Rosenfeld et al., *Cell* 68:143-155 (1992); Mastrangeli et al., *J. Clin. Invest.* 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., *Gene Therapy* 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., *Proc. Soc. Exp. Biol. Med.* 204:289-300 (1993); U.S. Patent No. 5,436,146).

Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method

known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes  
5 into cells (see, e.g., Loeffler and Behr, *Meth. Enzymol.* 217:599-618 (1993); Cohen et al., *Meth. Enzymol.* 217:618-644 (1993); Cline, *Pharmac. Ther.* 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is  
10 expressible by the cell and preferably heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

15 Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as Tlymphocytes, Blymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic  
20 stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody are introduced into the cells such that they are expressible  
25 by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, *Cell* 71:973-985 (1992); Rheinwald, *Meth. Cell Bio.*  
30 21A:229 (1980); and Pittelkow and Scott, *Mayo Clinic Proc.* 61:771 (1986)).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that

expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription. Demonstration of Therapeutic or Prophylactic Activity

The compounds or pharmaceutical compositions of the invention are preferably tested in vitro, and then in vivo for the desired therapeutic or prophylactic activity, prior to use in humans. For example, in vitro assays to demonstrate the therapeutic or prophylactic utility of a compound or pharmaceutical composition include, the effect of a compound on a cell line or a patient tissue sample. The effect of the compound or composition on the cell line and/or tissue sample can be determined utilizing techniques known to those of skill in the art including, but not limited to, rosette formation assays and cell lysis assays. In accordance with the invention, in vitro assays which can be used to determine whether administration of a specific compound is indicated, include in vitro cell culture assays in which a patient tissue sample is grown in culture, and exposed to or otherwise administered a compound, and the effect of such compound upon the tissue sample is observed.

#### 15 *Therapeutic/Prophylactic Administration and Composition*

The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical composition of the invention, preferably a polypeptide or antibody of the invention. In a preferred aspect, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce undesired side-effects). The subject is preferably an animal, including but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.

Formulations and methods of administration that can be employed when the compound comprises a nucleic acid or an immunoglobulin are described above; additional appropriate formulations and routes of administration can be selected from among those described herein below.

Various delivery systems are known and can be used to administer a compound of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the compound, receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral

routes. The compounds or compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when administering a protein, including an antibody, of the invention, care must be taken to use materials to which the protein does not absorb.

In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, *Science* 249:1527-1533 (1990); Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353- 365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton, *CRC Crit. Ref. Biomed. Eng.* 14:201 (1987); Buchwald et al., *Surgery* 88:507 (1980); Saudek et al., *N. Engl. J. Med.* 321:574 (1989)). In another embodiment, polymeric materials can be used (see *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., *Macromol. Sci. Rev. Macromol. Chem.* 23:61 (1983); see also Levy et al., *Science* 228:190 (1985); During et al., *Ann. Neurol.* 25:351 (1989); Howard et al.,

J.Neurosurg. 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, supra, vol. 2, pp. 115-138 (1984)).

5 Other controlled release systems are discussed in the review by Langer (Science 249:1527-1533 (1990)).

In a specific embodiment where the compound of the invention is a nucleic acid encoding a protein, the nucleic acid can be administered in vivo to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector  
10 and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox- like peptide which is known to enter the nucleus (see e.g., Joliot et al., Proc. Natl. Acad. Sci. USA 88:1864-1868  
15 (1991)), etc. Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means  
20 approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic  
25 origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate,  
30 glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form



of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compounds of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend

on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

5 For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life  
10 foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the antibodies by modifications such as, for example, lipidation.

The invention also provides a pharmaceutical pack or kit comprising one or more  
15 containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

20

### ***Diagnosis and Imaging***

Labeled antibodies, and derivatives and analogs thereof, which specifically bind to a polypeptide of interest can be used for diagnostic purposes to detect, diagnose, or monitor diseases, disorders, and/or conditions associated with the aberrant expression and/or activity  
25 of a polypeptide of the invention. The invention provides for the detection of aberrant expression of a polypeptide of interest, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide  
30 gene expression level compared to the standard expression level is indicative of aberrant expression.

The invention provides a diagnostic assay for diagnosing a disorder, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a particular disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Antibodies of the invention can be used to assay protein levels in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine ( $^{125}\text{I}$ ,  $^{121}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{112}\text{In}$ ), and technetium ( $^{99}\text{Tc}$ ); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

One aspect of the invention is the detection and diagnosis of a disease or disorder associated with aberrant expression of a polypeptide of interest in an animal, preferably a mammal and most preferably a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled molecule which specifically binds to the polypeptide of interest; b) waiting for a time interval following the administering for permitting the labeled molecule to preferentially concentrate at sites in the subject where the polypeptide is expressed (and for unbound labeled molecule to be cleared to background level); c) determining background level; and d) detecting the labeled molecule in the subject, such that detection of labeled molecule above the background level indicates that the subject has a particular disease or disorder associated with aberrant expression of the polypeptide of interest. Background level can be determined by various methods including, comparing the

amount of labeled molecule detected to a standard value previously determined for a particular system.

It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of  $^{99m}\text{Tc}$ . The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).

Depending on several variables, including the type of label used and the mode of administration, the time interval following the administration for permitting the labeled molecule to preferentially concentrate at sites in the subject and for unbound labeled molecule to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5 to 20 days or 5 to 10 days.

In an embodiment, monitoring of the disease or disorder is carried out by repeating the method for diagnosing the disease or disease, for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, etc.

Presence of the labeled molecule can be detected in the patient using methods known in the art for in vivo scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods of the invention include, but are not limited to, computed tomography (CT), whole body scan such as position emission tomography (PET), magnetic resonance imaging (MRI), and sonography.

In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston et al., U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patient using positron emission-tomography. In yet another embodiment, the molecule

is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

### *Kits*

5           The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises an antibody of the invention, preferably a purified antibody, in one or more containers. In a specific embodiment, the kits of the present invention contain a substantially isolated polypeptide comprising an epitope which is specifically immunoreactive with an antibody included in the kit. Preferably, the kits of the present  
10           invention further comprise a control antibody which does not react with the polypeptide of interest. In another specific embodiment, the kits of the present invention contain a means for detecting the binding of an antibody to a polypeptide of interest (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes  
15           the first antibody may be conjugated to a detectable substrate).

          In another specific embodiment of the present invention, the kit is a diagnostic kit for use in screening serum containing antibodies specific against proliferative and/or cancerous polynucleotides and polypeptides. Such a kit may include a control antibody that does not react with the polypeptide of interest. Such a kit may include a substantially isolated  
20           polypeptide antigen comprising an epitope which is specifically immunoreactive with at least one anti-polypeptide antigen antibody. Further, such a kit includes means for detecting the binding of said antibody to the antigen (e.g., the antibody may be conjugated to a fluorescent compound such as fluorescein or rhodamine which can be detected by flow cytometry). In specific embodiments, the kit may include a recombinantly produced or chemically  
25           synthesized polypeptide antigen. The polypeptide antigen of the kit may also be attached to a solid support.

          In a more specific embodiment the detecting means of the above-described kit includes a solid support to which said polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of  
30           the antibody to the polypeptide antigen can be detected by binding of the said reporter-labeled antibody.

In an additional embodiment, the invention includes a diagnostic kit for use in screening serum containing antigens of the polypeptide of the invention. The diagnostic kit includes a substantially isolated antibody specifically immunoreactive with polypeptide or polynucleotide antigens, and means for detecting the binding of the polynucleotide or polypeptide antigen to the antibody. In one embodiment, the antibody is attached to a solid support. In a specific embodiment, the antibody may be a monoclonal antibody. The detecting means of the kit may include a second, labeled monoclonal antibody. Alternatively, or in addition, the detecting means may include a labeled, competing antigen.

In one diagnostic configuration, test serum is reacted with a solid phase reagent having a surface-bound antigen obtained by the methods of the present invention. After binding with specific antigen antibody to the reagent and removing unbound serum components by washing, the reagent is reacted with reporter-labeled anti-human antibody to bind reporter to the reagent in proportion to the amount of bound anti-antigen antibody on the solid support. The reagent is again washed to remove unbound labeled antibody, and the amount of reporter associated with the reagent is determined. Typically, the reporter is an enzyme which is detected by incubating the solid phase in the presence of a suitable fluorometric, luminescent or colorimetric substrate (Sigma, St. Louis, MO).

The solid surface reagent in the above assay is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plate or filter material. These attachment methods generally include non-specific adsorption of the protein to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

Thus, the invention provides an assay system or kit for carrying out this diagnostic method. The kit generally includes a support with surface-bound recombinant antigens, and a reporter-labeled anti-human antibody for detecting surface-bound anti-antigen antibody.

#### **Uses of the Polynucleotides**

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The breast/ovarian cancer antigen polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each sequence is specifically targeted to and can hybridize with a particular location on an individual human chromosome, thus each polynucleotide of the present invention can routinely be used as a chromosome marker using techniques known in the art.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably at least 15 bp (e.g., 15-25 bp) from the sequences shown in SEQ ID NO:X, or the complement thereto. Primers can optionally be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, preselection by hybridization to construct chromosome specific-cDNA libraries, and computer mapping techniques (See, e.g., Shuler, Trends Biotechnol 16:456-459 (1998) which is hereby incorporated by reference in its entirety).

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes).

Thus, the present invention also provides a method for chromosomal localization which involves (a) preparing PCR primers from the polynucleotide sequences in Table 3 and SEQ ID NO:X and (b) screening somatic cell hybrids containing individual chromosomes.

The polynucleotides of the present invention would likewise be useful for radiation  
5 hybrid mapping, HAPPY mapping, and long range restriction mapping. For a review of these techniques and others known in the art, see, e.g. Dear, "Genome Mapping: A Practical Approach," IRL Press at Oxford University Press, London (1997); Aydin, J. Mol. Med. 77:691-694 (1999); Hacia et al., Mol. Psychiatry 3:483-492 (1998); Herrick et al., Chromosome Res. 7:409-423 (1999); Hamilton et al., Methods Cell Biol. 62:265-280 (2000);  
10 and/or Ott, J. Hered. 90:68-70 (1999) each of which is hereby incorporated by reference in its entirety.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular  
15 disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library).) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

20 Thus, once coinheritance is established, differences in a polynucleotide of the invention and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all  
25 affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

30 Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using the polynucleotides of the



invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

Thus, the invention provides a method of detecting increased or decreased expression levels of the breast, ovarian, breast cancer and/or ovarian cancer polynucleotides in affected individuals as compared to unaffected individuals using polynucleotides of the present invention and techniques known in the art, including but not limited to the method described in Example 11. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

Thus, the invention also provides a diagnostic method useful during diagnosis of a disorder related to the female reproductive system, particularly a disorder related to the breast and/or ovary, including breast cancer and/or ovarian cancer, involving measuring the expression level of breast/ovarian cancer antigen polynucleotides in breast and/or ovarian tissue or other cells or body fluid from an individual and comparing the measured gene expression level with a standard breast, ovarian, breast cancer and/or ovarian cancer polynucleotide expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a disorder related to the female reproductive system, particularly a disorder related to the breast and/or ovary, including breast cancer and/or ovarian cancer.

In still another embodiment, the invention includes a kit for analyzing samples for the presence of proliferative and/or cancerous polynucleotides derived from a test subject. In a general embodiment, the kit includes at least one polynucleotide probe containing a nucleotide sequence that will specifically hybridize with a polynucleotide of the invention and a suitable container. In a specific embodiment, the kit includes two polynucleotide probes defining an internal region of the polynucleotide of the invention, where each probe has one strand containing a 31'-mer-end internal to the region. In a further embodiment, the probes may be useful as primers for polymerase chain reaction amplification.

Where a diagnosis of a disorder related to the female reproductive system, particularly a disorder related to the breast and/or ovary, including, for example, diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed breast, ovarian, breast cancer and/or ovarian cancer polynucleotide expression will experience a

worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

By "measuring the expression level of breast, ovarian, breast cancer and/or ovarian cancer polynucleotides" is intended qualitatively or quantitatively measuring or estimating the level of the breast, ovarian, breast cancer and/or ovarian cancer polypeptide or the level of the mRNA encoding the breast, ovarian, breast cancer and/or ovarian cancer polypeptide in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the breast, ovarian, breast cancer and/or ovarian cancer polypeptide level or mRNA level in a second biological sample). Preferably, the breast, ovarian, breast cancer and/or ovarian cancer polypeptide level or mRNA level in the first biological sample is measured or estimated and compared to a standard breast, ovarian, breast cancer and/or ovarian cancer polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the female reproductive system related disorder or being determined by averaging levels from a population of individuals not having a female reproductive system related disorder. As will be appreciated in the art, once a standard breast, ovarian, breast cancer and/or ovarian cancer polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

By "biological sample" is intended any biological sample obtained from an individual, body fluid, cell line, tissue culture, or other source which contains breast, ovarian, breast cancer and/or ovarian cancer polypeptide or the corresponding mRNA. As indicated, biological samples include body fluids (such as vaginal pool, breast milk, lymph, sera, plasma, urine, semen, synovial fluid and spinal fluid) which contain the breast, ovarian, breast cancer and/or ovarian cancer polypeptide, breast and/or ovarian tissue, and other tissue sources found to express the breast, ovarian, breast cancer and/or ovarian cancer polypeptide. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

The method(s) provided above may preferably be applied in a diagnostic method and/or kits in which polynucleotides and/or polypeptides of the invention are attached to a solid support. In one exemplary method, the support may be a "gene chip" or a "biological chip" as described in US Patents 5,837,832, 5,874,219, and 5,856,174. Further, such a gene chip with breast, ovarian, breast cancer and/or ovarian cancer polynucleotides attached may

be used to identify polymorphisms between the breast, ovarian, breast cancer and/or ovarian cancer polynucleotide sequences, with polynucleotides isolated from a test subject. The knowledge of such polymorphisms (i.e. their location, as well as, their existence) would be beneficial in identifying disease loci for many disorders, such as for example, in neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions, though most preferably in breast and/or ovarian related proliferative, and/or cancerous diseases and conditions. Such a method is described in US Patents 5,858,659 and 5,856,104. The US Patents referenced supra are hereby incorporated by reference in their entirety herein.

The present invention encompasses breast, ovarian, breast cancer and/or ovarian cancer polynucleotides that are chemically synthesized, or reproduced as peptide nucleic acids (PNA), or according to other methods known in the art. The use of PNAs would serve as the preferred form if the polynucleotides of the invention are incorporated onto a solid support, or gene chip. For the purposes of the present invention, a peptide nucleic acid (PNA) is a polyamide type of DNA analog and the monomeric units for adenine, guanine, thymine and cytosine are available commercially (Perceptive Biosystems). Certain components of DNA, such as phosphorus, phosphorus oxides, or deoxyribose derivatives, are not present in PNAs. As disclosed by P. E. Nielsen, M. Egholm, R. H. Berg and O. Buchardt, Science 254, 1497 (1991); and M. Egholm, O. Buchardt, L. Christensen, C. Behrens, S. M. Freier, D. A. Driver, R. H. Berg, S. K. Kim, B. Norden, and P. E. Nielsen, Nature 365, 666 (1993), PNAs bind specifically and tightly to complementary DNA strands and are not degraded by nucleases. In fact, PNA binds more strongly to DNA than DNA itself does. This is probably because there is no electrostatic repulsion between the two strands, and also the polyamide backbone is more flexible. Because of this, PNA/DNA duplexes bind under a wider range of stringency conditions than DNA/DNA duplexes, making it easier to perform multiplex hybridization. Smaller probes can be used than with DNA due to the strong binding. In addition, it is more likely that single base mismatches can be determined with PNA/DNA hybridization because a single mismatch in a PNA/DNA 15-mer lowers the melting point ( $T_{sub.m}$ ) by 8°-20° C, vs. 4°-16° C for the DNA/DNA 15-mer duplex. Also, the absence of charge groups in PNA means that hybridization can be done at low ionic strengths and reduce possible interference by salt during the analysis.

The present invention have uses which include, but are not limited to, detecting cancer in mammals. In particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: acute myelogenous leukemias including acute monocytic leukemia, acute myeloblastic leukemia, acute promyelocytic leukemia, acute myelomonocytic leukemia, acute erythroleukemia, acute megakaryocytic leukemia, and acute undifferentiated leukemia, etc.; and chronic myelogenous leukemias including chronic myelomonocytic leukemia, chronic granulocytic leukemia, etc. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

Pathological cell proliferative disorders are often associated with inappropriate activation of proto-oncogenes. (Gelmann, E. P. et al., "The Etiology of Acute Leukemia: Molecular Genetics and Viral Oncology," in *Neoplastic Diseases of the Blood*, Vol 1., Wiernik, P. H. et al. eds., 161-182 (1985)). Neoplasias are now believed to result from the qualitative alteration of a normal cellular gene product, or from the quantitative modification of gene expression by insertion into the chromosome of a viral sequence, by chromosomal translocation of a gene to a more actively transcribed region, or by some other mechanism. (Gelmann et al., supra) It is likely that mutated or altered expression of specific genes is involved in the pathogenesis of some leukemias, among other tissues and cell types. (Gelmann et al., supra) Indeed, the human counterparts of the oncogenes involved in some animal neoplasias have been amplified or translocated in some cases of human leukemia and carcinoma. (Gelmann et al., supra)

For example, c-myc expression is highly amplified in the non-lymphocytic leukemia cell line HL-60. When HL-60 cells are chemically induced to stop proliferation, the level of c-myc is found to be downregulated. (International Publication Number WO 91/15580). However, it has been shown that exposure of HL-60 cells to a DNA construct that is complementary to the 5' end of c-myc or c-myb blocks translation of the corresponding mRNAs which downregulates expression of the c-myc or c-myb proteins and causes arrest of cell proliferation and differentiation of the treated cells. (International Publication Number WO 91/15580; Wickstrom et al., *Proc. Natl. Acad. Sci.* 85:1028 (1988); Anfossi et al., *Proc. Natl. Acad. Sci.* 86:3379 (1989)). However, the skilled artisan would appreciate the present invention's usefulness is not limited to treatment of proliferative disorders of hematopoietic

cells and tissues, in light of the numerous cells and cell types of varying origins which are known to exhibit proliferative phenotypes.

In addition to the foregoing, a breast/ovarian cancer antigen polynucleotide can be used to control gene expression through triple helix formation or through antisense DNA or RNA. Antisense techniques are discussed, for example, in Okano, J. *Neurochem.* 56: 560 (1991); "Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance Lee et al., *Nucleic Acids Research* 6: 3073 (1979); Cooney et al., *Science* 241: 456 (1988); and Dervan et al., *Science* 251: 1360 (1991). Both methods rely on binding of the polynucleotide to a complementary DNA or RNA. For these techniques, preferred polynucleotides are usually oligonucleotides 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., *Nucl. Acids Res.* 6:3073 (1979); Cooney et al., *Science* 241:456 (1988); and Dervan et al., *Science* 251:1360 (1991) ) or to the mRNA itself (antisense - Okano, J. *Neurochem.* 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. The oligonucleotide described above can also be delivered to cells such that the antisense RNA or DNA may be expressed in vivo to inhibit production of polypeptide of the present invention antigens. Both techniques are effective in model systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease, and in particular, for the treatment of proliferative diseases and/or conditions.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed

on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

5       The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA  
10 sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues,  
15 e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, synovial fluid, amniotic fluid, breast milk, lymph, pulmonary sputum or surfactant, urine, fecal matter, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific  
20 polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular  
25 tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to breast, ovarian, breast cancer and/or ovarian cancer polynucleotides prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue  
30 cultures for contamination.

The polynucleotides of the present invention are also useful as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample.

Similarly, polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In addition, for a number of disorders of the above tissues or cells, significantly higher or lower  
5 levels of gene expression of the polynucleotides/polypeptides of the present invention may be detected in certain tissues (e.g., tissues expressing polypeptides and/or polynucleotides of the present invention, breast, ovarian, breast cancer and/or ovarian cancer tissues and/or cancerous and/or wounded tissues) or bodily fluids (e.g., vaginal pool, breast milk, serum, plasma, urine, synovial fluid or spinal fluid) taken from an individual having such a disorder,  
10 relative to a "standard" gene expression level, i.e., the expression level in healthy tissue from an individual not having the disorder.

Thus, the invention provides a diagnostic method of a disorder, which involves: (a) assaying gene expression level in cells or body fluid of an individual; (b) comparing the gene expression level with a standard gene expression level, whereby an increase or decrease in  
15 the assayed gene expression level compared to the standard expression level is indicative of a disorder.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the  
20 process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

#### **Uses of the Polypeptides**

25 Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

Polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays such as, for example, ABC immunoperoxidase (Hsu et al., J.  
30 Histochem. Cytochem. 29:577-580 (1981)) or cell type(s) (e.g., immunocytochemistry assays).

Antibodies can be used to assay levels of polypeptides encoded by polynucleotides of the invention in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for  
 5 detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine ( $^{131}\text{I}$ ,  $^{125}\text{I}$ ,  $^{123}\text{I}$ ,  $^{121}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{115\text{m}}\text{In}$ ,  $^{113\text{m}}\text{In}$ ,  $^{112}\text{In}$ ,  $^{111}\text{In}$ ), and technetium ( $^{99}\text{Tc}$ ,  $^{99\text{m}}\text{Tc}$ ), thallium ( $^{201}\text{Ti}$ ), gallium  
 10 ( $^{68}\text{Ga}$ ,  $^{67}\text{Ga}$ ), palladium ( $^{103}\text{Pd}$ ), molybdenum ( $^{99}\text{Mo}$ ), xenon ( $^{133}\text{Xe}$ ), fluorine ( $^{18}\text{F}$ ),  $^{153}\text{Sm}$ ,  $^{177}\text{Lu}$ ,  $^{159}\text{Gd}$ ,  $^{149}\text{Pm}$ ,  $^{140}\text{La}$ ,  $^{175}\text{Yb}$ ,  $^{166}\text{Ho}$ ,  $^{90}\text{Y}$ ,  $^{47}\text{Sc}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{142}\text{Pr}$ ,  $^{105}\text{Rh}$ ,  $^{97}\text{Ru}$ ; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying levels of polypeptide of the present invention in a biological  
 15 sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be  
 20 incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example,  $^{131}\text{I}$ ,  $^{112}\text{In}$ ,  $^{99\text{m}}\text{Tc}$ , ( $^{131}\text{I}$ ,  $^{125}\text{I}$ ,  $^{123}\text{I}$ ,  $^{121}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{115\text{m}}\text{In}$ ,  $^{113\text{m}}\text{In}$ ,  $^{112}\text{In}$ ,  $^{111}\text{In}$ ), and technetium ( $^{99}\text{Tc}$ ,  $^{99\text{m}}\text{Tc}$ ), thallium ( $^{201}\text{Ti}$ ), gallium ( $^{68}\text{Ga}$ ,  $^{67}\text{Ga}$ ), palladium ( $^{103}\text{Pd}$ ),  
 25 molybdenum ( $^{99}\text{Mo}$ ), xenon ( $^{133}\text{Xe}$ ), fluorine ( $^{18}\text{F}$ ,  $^{153}\text{Sm}$ ,  $^{177}\text{Lu}$ ,  $^{159}\text{Gd}$ ,  $^{149}\text{Pm}$ ,  $^{140}\text{La}$ ,  $^{175}\text{Yb}$ ,  $^{166}\text{Ho}$ ,  $^{90}\text{Y}$ ,  $^{47}\text{Sc}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{142}\text{Pr}$ ,  $^{105}\text{Rh}$ ,  $^{97}\text{Ru}$ ), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for immune system disorder. It will be understood in the art that the size of the subject and the imaging system  
 30 used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of  $^{99\text{m}}\text{Tc}$ . The labeled antibody or



antibody fragment will then preferentially accumulate at the location of cells which express the polypeptide encoded by a polynucleotide of the invention. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in *Tumor Imaging: The Radiochemical Detection of Cancer*, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.

By "toxin" is meant one or more compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNase, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. "Toxin" also includes a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example,  $^{213}\text{Bi}$ , or other radioisotopes such as, for example,  $^{103}\text{Pd}$ ,  $^{133}\text{Xe}$ ,  $^{131}\text{I}$ ,  $^{68}\text{Ge}$ ,  $^{57}\text{Co}$ ,  $^{65}\text{Zn}$ ,  $^{85}\text{Sr}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{90}\text{Y}$ ,  $^{153}\text{Sm}$ ,  $^{153}\text{Gd}$ ,  $^{169}\text{Yb}$ ,  $^{51}\text{Cr}$ ,  $^{54}\text{Mn}$ ,  $^{75}\text{Se}$ ,  $^{113}\text{Sn}$ ,  $^{90}\text{Yttrium}$ ,  $^{117}\text{Tin}$ ,  $^{186}\text{Rhenium}$ ,  $^{166}\text{Holmium}$ , and  $^{188}\text{Rhenium}$ ; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

Techniques known in the art may be applied to label polypeptides of the invention (including antibodies). Such techniques include, but are not limited to, the use of bifunctional conjugating agents (see e.g., U.S. Patent Nos. 5,756,065; 5,714,631; 5,696,239; 5,652,361; 5,505,931; 5,489,425; 5,435,990; 5,428,139; 5,342,604; 5,274,119; 4,994,560; 5 and 5,808,003; the contents of each of which are hereby incorporated by reference in its entirety).

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression level of a breast, ovarian, breast cancer and/or ovarian cancer polypeptide of the present invention in cells or body fluid of an individual, or more  
10 preferably, assaying the expression level of a breast, ovarian, breast cancer and/or ovarian cancer of the present invention in breast and/or ovarian cells or vaginal pool or breast milk of an individual; and (b) comparing the assayed polypeptide expression level with a standard polypeptide expression level, whereby an increase or decrease in the assayed polypeptide expression level compared to the standard expression level is indicative of a disorder. With  
15 respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or  
20 further progression of the cancer.

Moreover, breast/ovarian cancer antigen polypeptides of the present invention can be used to treat or prevent diseases or conditions such as, for example, neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or  
25 cancerous diseases and conditions, preferably proliferative disorders of the breast and/or ovary, and/or cancerous disease and conditions. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B, SOD, catalase, DNA repair proteins), to inhibit the  
30 activity of a polypeptide (e.g., an oncogene or tumor suppressor), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing

inflammation), or to bring about a desired response (e.g., blood vessel growth inhibition, enhancement of the immune response to proliferative cells or tissues).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease (as described supra, and elsewhere herein). For example, administration of an antibody directed to a polypeptide of the present invention can bind, and/or neutralize the polypeptide, and/or reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

#### Gene Therapy Methods

Another aspect of the present invention is to gene therapy methods for treating or preventing disorders, diseases and conditions. The gene therapy methods relate to the introduction of nucleic acid (DNA, RNA and antisense DNA or RNA) sequences into an animal to achieve expression of the polypeptide of the present invention. This method requires a polynucleotide which codes for a polypeptide of the present invention operatively linked to a promoter and any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques are known in the art, see, for example, WO90/11092, which is herein incorporated by reference.

Thus, for example, cells from a patient may be engineered with a polynucleotide (DNA or RNA) comprising a promoter operably linked to a polynucleotide of the present invention ex vivo, with the engineered cells then being provided to a patient to be treated with the polypeptide of the present invention. Such methods are well-known in the art. For example, see Belldgrun, A., et al., J. Natl. Cancer Inst. 85: 207-216 (1993); Ferrantini, M. et al., Cancer Research 53: 1107-1112 (1993); Ferrantini, M. et al., J. Immunology 153: 4604-4615 (1994); Kaido, T., et al., Int. J. Cancer 60: 221-229 (1995); Ogura, H., et al., Cancer Research 50: 5102-5106 (1990); Santodonato, L., et al., Human Gene Therapy 7:1-10 (1996);

Santodonato, L., et al., Gene Therapy 4:1246-1255 (1997); and Zhang, J.-F. et al., Cancer Gene Therapy 3: 31-38 (1996)), which are herein incorporated by reference. In one embodiment, the cells which are engineered are arterial cells. The arterial cells may be reintroduced into the patient through direct injection to the artery, the tissues surrounding the  
5 artery, or through catheter injection.

As discussed in more detail below, the polynucleotide constructs can be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, and the like). The polynucleotide constructs may be delivered in a pharmaceutically acceptable liquid or  
10 aqueous carrier.

In one embodiment, the polynucleotide of the present invention is delivered as a naked polynucleotide. The term "naked" polynucleotide, DNA or RNA refers to sequences that are free from any delivery vehicle that acts to assist, promote or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or  
15 precipitating agents and the like. However, the polynucleotide of the present invention can also be delivered in liposome formulations and lipofectin formulations and the like can be prepared by methods well known to those skilled in the art. Such methods are described, for example, in U.S. Patent Nos. 5,593,972, 5,589,466, and 5,580,859, which are herein incorporated by reference.

The polynucleotide vector constructs used in the gene therapy method are preferably  
20 constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Appropriate vectors include pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; pSVK3, pBPV, pMSG and pSVL available from Pharmacia; and pEF1/V5, pcDNA3.1, and pRc/CMV2 available from Invitrogen. Other suitable vectors  
25 will be readily apparent to the skilled artisan.

Any strong promoter known to those skilled in the art can be used for driving the expression of the polynucleotide sequence. Suitable promoters include adenoviral promoters, such as the adenoviral major late promoter; or heterologous promoters, such as the cytomegalovirus (CMV) promoter; the respiratory syncytial virus (RSV) promoter; inducible  
30 promoters, such as the MMT promoter, the metallothionein promoter; heat shock promoters; the albumin promoter; the ApoA1 promoter; human globin promoters; viral thymidine kinase promoters, such as the Herpes Simplex thymidine kinase promoter; retroviral LTRs; the b-

actin promoter; and human growth hormone promoters. The promoter also may be the native promoter for the polynucleotide of the present invention.

Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular, fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked nucleic acid sequence injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 mg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration.

The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues,

throat or mucous membranes of the nose. In addition, naked DNA constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The naked polynucleotides are delivered by any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical  
5 administration, catheter infusion, and so-called "gene guns". These delivery methods are known in the art.

The constructs may also be delivered with delivery vehicles such as viral sequences, viral particles, liposome formulations, lipofectin, precipitating agents, etc. Such methods of delivery are known in the art.

10 In certain embodiments, the polynucleotide constructs are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations. However, cationic liposomes are particularly preferred because a tight charge complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have  
15 been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA (1989) 86:6077-6081, which is herein incorporated by reference); and purified transcription factors (Debs et al., J. Biol. Chem. (1990) 265:10189-10192, which is herein incorporated by reference), in functional form.

20 Cationic liposomes are readily available. For example, N[1-2,3-dioleoyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are particularly useful and are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, N.Y. (See, also, Felgner et al., Proc. Natl Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference). Other commercially available liposomes include  
25 transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication No. WO 90/11092 (which is herein incorporated by reference) for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes  
30 is explained in the literature, see, e.g., P. Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417, which is herein incorporated by reference. Similar methods can be used to prepare liposomes from other cationic lipid materials.

Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl, choline, cholesterol, phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG),  
5 dioleoylphosphatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP starting materials in appropriate ratios. Methods for making liposomes using these materials are well known in the art.

For example, commercially dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can  
10 be used in various combinations to make conventional liposomes, with or without the addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat  
15 Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

20 The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome-nucleic acid complexes are prepared using methods well known in the art. See, e.g., Straubinger et al., *Methods of Immunology* (1983), 101:512-527, which is herein incorporated by reference. For example, MLVs containing nucleic acid can be prepared by  
25 depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate  
30 solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to

the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include  $\text{Ca}^{2+}$ -EDTA chelation (Papahadjopoulos et al., *Biochim. Biophys. Acta* (1975) 394:483; Wilson et al., *Cell* (1979) 17:77); ether injection (Deamer, D. and Bangham, A., *Biochim. Biophys. Acta* (1976) 443:629; Ostro et al., *Biochem. Biophys. Res. Commun.* (1977) 76:836; Fraley et al., *Proc. Natl. Acad. Sci. USA* (1979) 76:3348); detergent dialysis (Enoch, H. and Strittmatter, P., *Proc. Natl. Acad. Sci. USA* (1979) 76:145); and reverse-phase evaporation (REV) (Fraley et al., *J. Biol. Chem.* (1980) 255:10431; Szoka, F. and Papahadjopoulos, D., *Proc. Natl. Acad. Sci. USA* (1978) 75:145; Schaefer-Ridder et al., *Science* (1982) 215:166), which are  
10 herein incorporated by reference.

Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ration will be from about 5:1 to about 1:5. More preferably, the ration will be about 3:1 to about 1:3. Still more preferably, the ratio will be about 1:1.

U.S. Patent No. 5,676,954 (which is herein incorporated by reference) reports on the  
15 injection of genetic material, complexed with cationic liposomes carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no.  
20 WO 94/9469 (which are herein incorporated by reference) provide methods for delivering DNA-cationic lipid complexes to mammals.

In certain embodiments, cells are engineered, ex vivo or in vivo, using a retroviral particle containing RNA which comprises a sequence encoding a polypeptide of the present invention. Retroviruses from which the retroviral plasmid vectors may be derived include,  
25 but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, Rous sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are  
30 not limited to, the PE501, PA317, R-2, R-AM, PA12, T19-14X, VT-19-17-H2, RCRE, RCRIP, GP+E-86, GP+envAm12, and DAN cell lines as described in Miller, *Human Gene Therapy* 1:5-14 (1990), which is incorporated herein by reference in its entirety. The vector



may transduce the packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and  $\text{CaPO}_4$  precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

5           The producer cell line generates infectious retroviral vector particles which include polynucleotide encoding a polypeptide of the present invention. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either in vitro or in vivo. The transduced eukaryotic cells will express a polypeptide of the present invention.

          In certain other embodiments, cells are engineered, ex vivo or in vivo, with  
10   polynucleotide contained in an adenovirus vector. Adenovirus can be manipulated such that it encodes and expresses a polypeptide of the present invention, and at the same time is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. Adenovirus expression is achieved without integration of the viral DNA into the host cell chromosome, thereby alleviating concerns about insertional mutagenesis. Furthermore, adenoviruses have  
15   been used as live enteric vaccines for many years with an excellent safety profile (Schwartz, A. R. et al. (1974) *Am. Rev. Respir. Dis.* 109:233-238). Finally, adenovirus mediated gene transfer has been demonstrated in a number of instances including transfer of alpha-1-antitrypsin and CFTR to the lungs of cotton rats (Rosenfeld, M. A. et al. (1991) *Science* 252:431-434; Rosenfeld et al., (1992) *Cell* 68:143-155). Furthermore, extensive  
20   studies to attempt to establish adenovirus as a causative agent in human cancer were uniformly negative (Green, M. et al. (1979) *Proc. Natl. Acad. Sci. USA* 76:6606).

          Suitable adenoviral vectors useful in the present invention are described, for example, in Kozarsky and Wilson, *Curr. Opin. Genet. Devel.* 3:499-503 (1993); Rosenfeld et al., *Cell* 68:143-155 (1992); Engelhardt et al., *Human Genet. Ther.* 4:759-769 (1993); Yang et al.,  
25   *Nature Genet.* 7:362-369 (1994); Wilson et al., *Nature* 365:691-692 (1993); and U.S. Patent No. 5,652,224, which are herein incorporated by reference. For example, the adenovirus vector Ad2 is useful and can be grown in human 293 cells. These cells contain the E1 region of adenovirus and constitutively express Ela and Elb, which complement the defective adenoviruses by providing the products of the genes deleted from the vector. In addition to  
30   Ad2, other varieties of adenovirus (e.g., Ad3, Ad5, and Ad7) are also useful in the present invention.

Preferably, the adenoviruses used in the present invention are replication deficient. Replication deficient adenoviruses require the aid of a helper virus and/or packaging cell line to form infectious particles. The resulting virus is capable of infecting cells and can express a polynucleotide of interest which is operably linked to a promoter, but cannot replicate in most cells. Replication deficient adenoviruses may be deleted in one or more of all or a portion of the following genes: E1a, E1b, E3, E4, E2a, or L1 through L5.

In certain other embodiments, the cells are engineered, ex vivo or in vivo, using an adeno-associated virus (AAV). AAVs are naturally occurring defective viruses that require helper viruses to produce infectious particles (Muzyczka, N., Curr. Topics in Microbiol. Immunol. 158:97 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells. Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate, but space for exogenous DNA is limited to about 4.5 kb. Methods for producing and using such AAVs are known in the art. See, for example, U.S. Patent Nos. 5,139,941, 5,173,414, 5,354,678, 5,436,146, 5,474,935, 5,478,745, and 5,589,377.

For example, an appropriate AAV vector for use in the present invention will include all the sequences necessary for DNA replication, encapsidation, and host-cell integration. The polynucleotide construct is inserted into the AAV vector using standard cloning methods, such as those found in Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (1989). The recombinant AAV vector is then transfected into packaging cells which are infected with a helper virus, using any standard technique, including lipofection, electroporation, calcium phosphate precipitation, etc. Appropriate helper viruses include adenoviruses, cytomegaloviruses, vaccinia viruses, or herpes viruses. Once the packaging cells are transfected and infected, they will produce infectious AAV viral particles which contain the polynucleotide construct. These viral particles are then used to transduce eukaryotic cells, either ex vivo or in vivo. The transduced cells will contain the polynucleotide construct integrated into its genome, and will express a polypeptide of the invention.

Another method of gene therapy involves operably associating heterologous control regions and endogenous polynucleotide sequences (e.g. encoding a polypeptide of the present invention) via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc.

Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not normally expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made, using standard techniques known in the art, which contain the promoter with targeting sequences flanking the promoter. Suitable promoters are described herein. The targeting sequence is sufficiently complementary to an endogenous sequence to permit homologous recombination of the promoter-targeting sequence with the endogenous sequence. The targeting sequence will be sufficiently near the 5' end of the desired endogenous polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination.

The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter. The amplified promoter and targeting sequences are digested and ligated together.

The promoter-targeting sequence construct is delivered to the cells, either as naked polynucleotide, or in conjunction with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, whole viruses, lipofection, precipitating agents, etc., described in more detail above. The P promoter-targeting sequence can be delivered by any method, included direct needle injection, intravenous injection, topical administration, catheter infusion, particle accelerators, etc. The methods are described in more detail below.

The promoter-targeting sequence construct is taken up by cells. Homologous recombination between the construct and the endogenous sequence takes place, such that an endogenous sequence is placed under the control of the promoter. The promoter then drives the expression of the endogenous sequence.

Preferably, the polynucleotide encoding a polypeptide of the present invention contains a secretory signal sequence that facilitates secretion of the protein. Typically, the signal sequence is positioned in the coding region of the polynucleotide to be expressed towards or at the 5' end of the coding region. The signal sequence may be homologous or heterologous to the polynucleotide of interest and may be homologous or heterologous to the

cells to be transfected. Additionally, the signal sequence may be chemically synthesized using methods known in the art.

Any mode of administration of any of the above-described polynucleotides constructs can be used so long as the mode results in the expression of one or more molecules in an amount sufficient to provide a therapeutic effect. This includes direct needle injection, systemic injection, catheter infusion, biolistic injectors, particle accelerators (i.e., "gene guns"), gelfoam sponge depots, other commercially available depot materials, osmotic pumps (e.g., Alza minipumps), oral or suppositorial solid (tablet or pill) pharmaceutical formulations, and decanting or topical applications during surgery. For example, direct injection of naked calcium phosphate-precipitated plasmid into rat liver and rat spleen or a protein-coated plasmid into the portal vein has resulted in gene expression of the foreign gene in the rat livers (Kaneda et al., Science 243:375 (1989)).

A preferred method of local administration is by direct injection. Preferably, a recombinant molecule of the present invention complexed with a delivery vehicle is administered by direct injection into or locally within the area of arteries. Administration of a composition locally within the area of arteries refers to injecting the composition centimeters and preferably, millimeters within arteries.

Another method of local administration is to contact a polynucleotide construct of the present invention in or around a surgical wound. For example, a patient can undergo surgery and the polynucleotide construct can be coated on the surface of tissue inside the wound or the construct can be injected into areas of tissue inside the wound.

Therapeutic compositions useful in systemic administration, include recombinant molecules of the present invention complexed to a targeted delivery vehicle of the present invention. Suitable delivery vehicles for use with systemic administration comprise liposomes comprising ligands for targeting the vehicle to a particular site.

Preferred methods of systemic administration, include intravenous injection, aerosol, oral and percutaneous (topical) delivery. Intravenous injections can be performed using methods standard in the art. Aerosol delivery can also be performed using methods standard in the art (see, for example, Stribling et al., Proc. Natl. Acad. Sci. USA 189:11277-11281, 1992, which is incorporated herein by reference). Oral delivery can be performed by complexing a polynucleotide construct of the present invention to a carrier capable of withstanding degradation by digestive enzymes in the gut of an animal. Examples of such

carriers, include plastic capsules or tablets, such as those known in the art. Topical delivery can be performed by mixing a polynucleotide construct of the present invention with a lipophilic reagent (e.g., DMSO) that is capable of passing into the skin.

Determining an effective amount of substance to be delivered can depend upon a number of factors including, for example, the chemical structure and biological activity of the substance, the age and weight of the animal, the precise condition requiring treatment and its severity, and the route of administration. The frequency of treatments depends upon a number of factors, such as the amount of polynucleotide constructs administered per dose, as well as the health and history of the subject. The precise amount, number of doses, and timing of doses will be determined by the attending physician or veterinarian.

Therapeutic compositions of the present invention can be administered to any animal, preferably to mammals and birds. Preferred mammals include humans, dogs, cats, mice, rats, rabbits sheep, cattle, horses and pigs, with humans being particularly preferred.

#### 15 **Biological Activities**

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, can be used in assays to test for one or more biological activities. If these polynucleotides or polypeptides, or agonists or antagonists of the present invention, do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides, and agonists or antagonists could be used to treat the associated disease.

#### **Immune Activity**

A polypeptide or polynucleotide, or agonists or antagonists of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, polynucleotides or polypeptides, or

agonists or antagonists of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells.

5 Polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g.  
10 agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

15 Moreover, polynucleotides or polypeptides, or agonists or antagonists of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia,  
20 factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, polynucleotides or polypeptides, or agonists or antagonists of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

25 Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of polynucleotides or polypeptides, or agonists or  
30 antagonists of the present invention that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitis, and autoimmune inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The administration of polynucleotides or polypeptides, or agonists or antagonists of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to modulate inflammation. For example, polynucleotides or polypeptides, or agonists or antagonists of the present invention may inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including chronic prostatitis, granulomatous prostatitis and malacoplakia, inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

**Hyperproliferative Disorders**

Polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used to treat or detect hyperproliferative disorders, including neoplasms. Polynucleotides or polypeptides, or agonists or antagonists of the present invention may  
5 inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, Polynucleotides or polypeptides, or agonists or antagonists of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing  
10 T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by  
15 Polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to neoplasms located in the: colon, abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

20 Similarly, other hyperproliferative disorders can also be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstrom's Macroglobulinemia, Gaucher's Disease,  
25 histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

One preferred embodiment utilizes polynucleotides of the present invention to inhibit aberrant cellular division, by gene therapy using the present invention, and/or protein fusions or fragments thereof.

30 Thus, the present invention provides a method for treating cell proliferative disorders by inserting into an abnormally proliferating cell a polynucleotide of the present invention, wherein said polynucleotide represses said expression.



Another embodiment of the present invention provides a method of treating cell-proliferative disorders in individuals comprising administration of one or more active gene copies of the present invention to an abnormally proliferating cell or cells. In a preferred embodiment, polynucleotides of the present invention is a DNA construct comprising a recombinant expression vector effective in expressing a DNA sequence encoding said polynucleotides. In another preferred embodiment of the present invention, the DNA construct encoding the polynucleotides of the present invention is inserted into cells to be treated utilizing a retrovirus, or more preferably an adenoviral vector (See G J. Nabel, et. al., PNAS 1999 96: 324-326, which is hereby incorporated by reference). In a most preferred embodiment, the viral vector is defective and will not transform non-proliferating cells, only proliferating cells. Moreover, in a preferred embodiment, the polynucleotides of the present invention inserted into proliferating cells either alone, or in combination with or fused to other polynucleotides, can then be modulated via an external stimulus (i.e. magnetic, specific small molecule, chemical, or drug administration, etc.), which acts upon the promoter upstream of said polynucleotides to induce expression of the encoded protein product. As such the beneficial therapeutic affect of the present invention may be expressly modulated (i.e. to increase, decrease, or inhibit expression of the present invention) based upon said external stimulus.

Polynucleotides of the present invention may be useful in repressing expression of oncogenic genes or antigens. By "repressing expression of the oncogenic genes " is intended the suppression of the transcription of the gene, the degradation of the gene transcript (pre-message RNA), the inhibition of splicing, the destruction of the messenger RNA, the prevention of the post-translational modifications of the protein, the destruction of the protein, or the inhibition of the normal function of the protein.

For local administration to abnormally proliferating cells, polynucleotides of the present invention may be administered by any method known to those of skill in the art including, but not limited to transfection, electroporation, microinjection of cells, or in vehicles such as liposomes, lipofectin, or as naked polynucleotides, or any other method described throughout the specification. The polynucleotide of the present invention may be delivered by known gene delivery systems such as, but not limited to, retroviral vectors (Gilboa, J. Virology 44:845 (1982); Hocke, Nature 320:275 (1986); Wilson, et al., Proc. Natl. Acad. Sci. U.S.A. 85:3014), vaccinia virus system (Chakrabarty et al., Mol. Cell Biol. 5:3403

(1985) or other efficient DNA delivery systems (Yates et al., Nature 313:812 (1985)) known to those skilled in the art. These references are exemplary only and are hereby incorporated by reference. In order to specifically deliver or transfect cells which are abnormally proliferating and spare non-dividing cells, it is preferable to utilize a retrovirus, or adenoviral  
5 (as described in the art and elsewhere herein) delivery system known to those of skill in the art. Since host DNA replication is required for retroviral DNA to integrate and the retrovirus will be unable to self replicate due to the lack of the retrovirus genes needed for its life cycle. Utilizing such a retroviral delivery system for polynucleotides of the present invention will target said gene and constructs to abnormally proliferating cells and will spare the non-  
10 dividing normal cells.

The polynucleotides of the present invention may be delivered directly to cell proliferative disorder/disease sites in internal organs, body cavities and the like by use of imaging devices used to guide an injecting needle directly to the disease site. The polynucleotides of the present invention may also be administered to disease sites at the time  
15 of surgical intervention.

By "cell proliferative disease" is meant any human or animal disease or disorder, affecting any one or any combination of organs, cavities, or body parts, which is characterized by single or multiple local abnormal proliferations of cells, groups of cells, or tissues, whether benign or malignant.

Any amount of the polynucleotides of the present invention may be administered as long as it has a biologically inhibiting effect on the proliferation of the treated cells. Moreover, it is possible to administer more than one of the polynucleotide of the present invention simultaneously to the same site. By "biologically inhibiting" is meant partial or total growth inhibition as well as decreases in the rate of proliferation or growth of the cells.  
20  
25 The biologically inhibitory dose may be determined by assessing the effects of the polynucleotides of the present invention on target malignant or abnormally proliferating cell growth in tissue culture, tumor growth in animals and cell cultures, or any other method known to one of ordinary skill in the art.

The present invention is further directed to antibody-based therapies which involve  
30 administering of anti-polypeptides and anti-polynucleotide antibodies to a mammalian, preferably human, patient for treating one or more of the described disorders. Methods for producing anti-polypeptides and anti-polynucleotide antibodies polyclonal and monoclonal

antibodies are described in detail elsewhere herein. Such antibodies may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

In particular, the antibodies, fragments and derivatives of the present invention are useful for treating a subject having or developing cell proliferative and/or differentiation disorders as described herein. Such treatment comprises administering a single or multiple doses of the antibody, or a fragment, derivative, or a conjugate thereof.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors, for example., which serve to increase the number or activity of effector cells which interact with the antibodies.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides, including fragments thereof. Preferred binding affinities include those with a dissociation constant or  $K_d$  less than  $5 \times 10^{-6}M$ ,  $10^{-6}M$ ,  $5 \times 10^{-7}M$ ,  $10^{-7}M$ ,  $5 \times 10^{-8}M$ ,  $10^{-8}M$ ,  $5 \times 10^{-9}M$ ,  $10^{-9}M$ ,  $5 \times 10^{-10}M$ ,  $10^{-10}M$ ,  $5 \times 10^{-11}M$ ,  $10^{-11}M$ ,  $5 \times 10^{-12}M$ ,  $10^{-12}M$ ,  $5 \times 10^{-13}M$ ,  $10^{-13}M$ ,  $5 \times 10^{-14}M$ ,  $10^{-14}M$ ,  $5 \times 10^{-15}M$ , and  $10^{-15}M$ .

Moreover, polypeptides of the present invention are useful in inhibiting the angiogenesis of proliferative cells or tissues, either alone, as a protein fusion, or in combination with other polypeptides directly or indirectly, as described elsewhere herein. In a most preferred embodiment, said anti-angiogenesis effect may be achieved indirectly, for example, through the inhibition of hematopoietic, tumor-specific cells, such as tumor-associated macrophages (See Joseph IB, et al. J Natl Cancer Inst, 90(21):1648-53 (1998),

which is hereby incorporated by reference). Antibodies directed to polypeptides or polynucleotides of the present invention may also result in inhibition of angiogenesis directly, or indirectly (See Witte L, et al., Cancer Metastasis Rev. 17(2):155-61 (1998), which is hereby incorporated by reference)).

5 Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a death-domain receptor, such as tumor necrosis factor (TNF) receptor-1, CD95 (Fas/APO-1), TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1  
10 and -2 (See Schulze-Osthoff K, et.al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides may induce apoptosis through other mechanisms, such as in the activation of other proteins which will activate apoptosis, or through stimulating the  
15 expression of said proteins, either alone or in combination with small molecule drugs or adjuvants, such as apoptonin, galectins, thioredoxins, antiinflammatory proteins (See for example, Mutat Res 400(1-2):447-55 (1998), Med Hypotheses.50(5):423-33 (1998), Chem Biol Interact. Apr 24;111-112:23-34 (1998), J Mol Med.76(6):402-12 (1998), Int J Tissue React;20(1):3-15 (1998), which are all hereby incorporated by reference).

20 Polypeptides, including protein fusions to, or fragments thereof, of the present invention are useful in inhibiting the metastasis of proliferative cells or tissues. Inhibition may occur as a direct result of administering polypeptides, or antibodies directed to said polypeptides as described elsewhere herein, or indirectly, such as activating the expression of proteins known to inhibit metastasis, for example alpha 4 integrins, (See, e.g., Curr Top  
25 Microbiol Immunol 1998;231:125-41, which is hereby incorporated by reference). Such therapeutic affects of the present invention may be achieved either alone, or in combination with small molecule drugs or adjuvants.

In another embodiment, the invention provides a method of delivering compositions containing the polypeptides of the invention (e.g., compositions containing polypeptides or  
30 polypeptide antibodies associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs) to targeted cells expressing the polypeptide of the present invention. Polypeptides or polypeptide antibodies of the invention may be associated with with

heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. Polypeptides, protein fusions to, or fragments thereof, of the present invention are useful in enhancing the immunogenicity and/or antigenicity of proliferating cells or tissues, either directly, such as would occur if the polypeptides of the present invention 'vaccinated' the immune response to respond to proliferative antigens and immunogens, or indirectly, such as in activating the expression of proteins known to enhance the immune response (e.g. chemokines), to said antigens and immunogens.

#### 10 **Cardiovascular Disorders**

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, may be used to treat cardiovascular disorders, including peripheral artery disease, such as limb ischemia.

Cardiovascular disorders include cardiovascular abnormalities, such as arterio-arterial fistula, arteriovenous fistula, cerebral arteriovenous malformations, congenital heart defects, pulmonary atresia, and Scimitar Syndrome. Congenital heart defects include aortic coarctation, cor triatriatum, coronary vessel anomalies, crisscross heart, dextrocardia, patent ductus arteriosus, Ebstein's anomaly, Eisenmenger complex, hypoplastic left heart syndrome, levocardia, tetralogy of fallot, transposition of great vessels, double outlet right ventricle, tricuspid atresia, persistent truncus arteriosus, and heart septal defects, such as aortopulmonary septal defect, endocardial cushion defects, Lutembacher's Syndrome, trilog  
y of Fallot, ventricular heart septal defects.

Cardiovascular disorders also include heart disease, such as arrhythmias, carcinoid heart disease, high cardiac output, low cardiac output, cardiac tamponade, endocarditis (including bacterial), heart aneurysm, cardiac arrest, congestive heart failure, congestive cardiomyopathy, paroxysmal dyspnea, cardiac edema, heart hypertrophy, congestive cardiomyopathy, left ventricular hypertrophy, right ventricular hypertrophy, post-infarction heart rupture, ventricular septal rupture, heart valve diseases, myocardial diseases, myocardial ischemia, pericardial effusion, pericarditis (including constrictive and tuberculous), pneumopericardium, postpericardiotomy syndrome, pulmonary heart disease, rheumatic heart disease, ventricular dysfunction, hyperemia, cardiovascular pregnancy complications, Scimitar Syndrome, cardiovascular syphilis, and cardiovascular tuberculosis.

Arrhythmias include sinus arrhythmia, atrial fibrillation, atrial flutter, bradycardia, extrasystole, Adams-Stokes Syndrome, bundle-branch block, sinoatrial block, long QT syndrome, parasystole, Lown-Ganong-Levine Syndrome, Mahaim-type pre-excitation syndrome, Wolff-Parkinson-White syndrome, sick sinus syndrome, tachycardias, and  
5 ventricular fibrillation. Tachycardias include paroxysmal tachycardia, supraventricular tachycardia, accelerated idioventricular rhythm, atrioventricular nodal reentry tachycardia, ectopic atrial tachycardia, ectopic junctional tachycardia, sinoatrial nodal reentry tachycardia, sinus tachycardia, Torsades de Pointes, and ventricular tachycardia.

Heart valve disease include aortic valve insufficiency, aortic valve stenosis, hear  
10 murmurs, aortic valve prolapse, mitral valve prolapse, tricuspid valve prolapse, mitral valve insufficiency, mitral valve stenosis, pulmonary atresia, pulmonary valve insufficiency, pulmonary valve stenosis, tricuspid atresia, tricuspid valve insufficiency, and tricuspid valve stenosis.

Myocardial diseases include alcoholic cardiomyopathy, congestive cardiomyopathy,  
15 hypertrophic cardiomyopathy, aortic subvalvular stenosis, pulmonary subvalvular stenosis, restrictive cardiomyopathy, Chagas cardiomyopathy, endocardial fibroelastosis, endomyocardial fibrosis, Kearns Syndrome, myocardial reperfusion injury, and myocarditis.

Myocardial ischemias include coronary disease, such as angina pectoris, coronary aneurysm, coronary arteriosclerosis, coronary thrombosis, coronary vasospasm, myocardial  
20 infarction and myocardial stunning.

Cardiovascular diseases also include vascular diseases such as aneurysms, angiodysplasia, angiomas, bacillary angiomas, Hippiel-Lindau Disease, Klippel-Trenaunay-Weber Syndrome, Sturge-Weber Syndrome, angioneurotic edema, aortic diseases, Takayasu's Arteritis, aortitis, Leriche's Syndrome, arterial occlusive diseases, arteritis,  
25 enarteritis, polyarteritis nodosa, cerebrovascular disorders, diabetic angiopathies, diabetic retinopathy, embolisms, thrombosis, erythromelalgia, hemorrhoids, hepatic veno-occlusive disease, hypertension, hypotension, ischemia, peripheral vascular diseases, phlebitis, pulmonary veno-occlusive disease, Raynaud's disease, CREST syndrome, retinal vein occlusion, Scimitar syndrome, superior vena cava syndrome, telangiectasia, atacia  
30 telangiectasia, hereditary hemorrhagic telangiectasia, varicocele, varicose veins, varicose ulcer, vasculitis, and venous insufficiency.

Aneurysms include dissecting aneurysms, false aneurysms, infected aneurysms, ruptured aneurysms, aortic aneurysms, cerebral aneurysms, coronary aneurysms, heart aneurysms, and iliac aneurysms.

Arterial occlusive diseases include arteriosclerosis, intermittent claudication, carotid stenosis, fibromuscular dysplasias, mesenteric vascular occlusion, Moyamoya disease, renal artery obstruction, retinal artery occlusion, and thromboangiitis obliterans.

Cerebrovascular disorders include carotid artery diseases, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformation, cerebral artery diseases, cerebral embolism and thrombosis, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, cerebral hemorrhage, epidural hematoma, subdural hematoma, subarachnoid hemorrhage, cerebral infarction, cerebral ischemia (including transient), subclavian steal syndrome, periventricular leukomalacia, vascular headache, cluster headache, migraine, and vertebrobasilar insufficiency.

Embolisms include air embolisms, amniotic fluid embolisms, cholesterol embolisms, blue toe syndrome, fat embolisms, pulmonary embolisms, and thromboembolisms. Thrombosis include coronary thrombosis, hepatic vein thrombosis, retinal vein occlusion, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, and thrombophlebitis.

Ischemia includes cerebral ischemia, ischemic colitis, compartment syndromes, anterior compartment syndrome, myocardial ischemia, reperfusion injuries, and peripheral limb ischemia. Vasculitis includes aortitis, arteritis, Behcet's Syndrome, Churg-Strauss Syndrome, mucocutaneous lymph node syndrome, thromboangiitis obliterans, hypersensitivity vasculitis, Schoenlein-Henoch purpura, allergic cutaneous vasculitis, and Wegener's granulomatosis.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, are especially effective for the treatment of critical limb ischemia and coronary disease.

Polypeptides may be administered using any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, biolistic injectors, particle accelerators, gelfoam sponge depots, other commercially available depot materials, osmotic pumps, oral or suppository solid pharmaceutical formulations, decanting or topical applications during surgery, aerosol delivery. Such methods are known in the art. Polypeptides may be administered as part of a

Therapeutic, described in more detail below. Methods of delivering polynucleotides are described in more detail herein.

#### Anti-Angiogenesis Activity

5       The naturally occurring balance between endogenous stimulators and inhibitors of angiogenesis is one in which inhibitory influences predominate. Rastinejad *et al.*, *Cell* 56:345-355 (1989). In those rare instances in which neovascularization occurs under normal physiological conditions, such as wound healing, organ regeneration, embryonic development, and female reproductive processes, angiogenesis is stringently regulated and  
10       spatially and temporally delimited. Under conditions of pathological angiogenesis such as that characterizing solid tumor growth, these regulatory controls fail. Unregulated angiogenesis becomes pathologic and sustains progression of many neoplastic and non-neoplastic diseases. A number of serious diseases are dominated by abnormal neovascularization including solid tumor growth and metastases, arthritis, some types of eye  
15       disorders, and psoriasis. See, e.g., reviews by Moses *et al.*, *Biotech.* 9:630-634 (1991); Folkman *et al.*, *N. Engl. J. Med.*, 333:1757-1763 (1995); Auerbach *et al.*, *J. Microvasc. Res.* 29:401-411 (1985); Folkman, *Advances in Cancer Research*, eds. Klein and Weinhouse, Academic Press, New York, pp. 175-203 (1985); Patz, *Am. J. Ophthalmol.* 94:715-743 (1982); and Folkman *et al.*, *Science* 221:719-725 (1983). In a number of pathological  
20       conditions, the process of angiogenesis contributes to the disease state. For example, significant data have accumulated which suggest that the growth of solid tumors is dependent on angiogenesis. Folkman and Klagsbrun, *Science* 235:442-447 (1987).

      The polynucleotides encoding a polypeptide of the present invention may be administered along with other polynucleotides encoding an angiogenic protein. Examples of  
25       angiogenic proteins include, but are not limited to, acidic and basic fibroblast growth factors, VEGF-1, VEGF-2, VEGF-3, epidermal growth factor alpha and beta, platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor alpha, hepatocyte growth factor, insulin like growth factor, colony stimulating factor, macrophage colony stimulating factor, granulocyte/macrophage colony stimulating factor, and nitric oxide  
30       synthase.

      The present invention provides for treatment of diseases or disorders associated with neovascularization by administration of the polynucleotides and/or polypeptides of the



invention, as well as agonists or antagonists of the present invention. Malignant and metastatic conditions which can be treated with the polynucleotides and polypeptides, or agonists or antagonists of the invention include, but are not limited to, malignancies, solid tumors, and cancers described herein and otherwise known in the art (for a review of such disorders, see Fishman *et al.*, Medicine, 2d Ed., J. B. Lippincott Co., Philadelphia (1985)). Thus, the present invention provides a method of treating an angiogenesis-related disease and/or disorder, comprising administering to an individual in need thereof a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist of the invention. For example, polynucleotides, polypeptides, antagonists and/or agonists may be utilized in a variety of additional methods in order to therapeutically treat a cancer or tumor. Cancers which may be treated with polynucleotides, polypeptides, antagonists and/or agonists include, but are not limited to solid tumors, including breast, ovarian, prostate, lung, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, thyroid cancer; primary tumors and metastases; melanomas; glioblastoma; Kaposi's sarcoma; leiomyosarcoma; non-small cell lung cancer; colorectal cancer; advanced malignancies; and blood born tumors such as leukemias. For example, polynucleotides, polypeptides, antagonists and/or agonists may be delivered topically, in order to treat cancers such as skin cancer, head and neck tumors, breast tumors, and Kaposi's sarcoma.

Within yet other aspects, polynucleotides, polypeptides, antagonists and/or agonists may be utilized to treat superficial forms of bladder cancer by, for example, intravesical administration. Polynucleotides, polypeptides, antagonists and/or agonists may be delivered directly into the tumor, or near the tumor site, via injection or a catheter. Of course, as the artisan of ordinary skill will appreciate, the appropriate mode of administration will vary according to the cancer to be treated. Other modes of delivery are discussed herein.

Polynucleotides, polypeptides, antagonists and/or agonists may be useful in treating other disorders, besides cancers, which involve angiogenesis. These disorders include, but are not limited to: benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid

arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque  
5 neovascularization; telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis.

For example, within one aspect of the present invention methods are provided for treating hypertrophic scars and keloids, comprising the step of administering a polynucleotide, polypeptide, antagonist and/or agonist of the invention to a hypertrophic scar  
10 or keloid.

Within one embodiment of the present invention polynucleotides, polypeptides, antagonists and/or agonists are directly injected into a hypertrophic scar or keloid, in order to prevent the progression of these lesions. This therapy is of particular value in the prophylactic treatment of conditions which are known to result in the development of  
15 hypertrophic scars and keloids (e.g., burns), and is preferably initiated after the proliferative phase has had time to progress (approximately 14 days after the initial injury), but before hypertrophic scar or keloid development. As noted above, the present invention also provides methods for treating neovascular diseases of the eye, including for example, corneal neovascularization, neovascular glaucoma, proliferative diabetic retinopathy, retrolental  
20 fibroplasia and macular degeneration.

Moreover, Ocular disorders associated with neovascularization which can be treated with the polynucleotides and polypeptides of the present invention (including agonists and/or antagonists) include, but are not limited to: neovascular glaucoma, diabetic retinopathy, retinoblastoma, retrolental fibroplasia, uveitis, retinopathy of prematurity macular  
25 degeneration, corneal graft neovascularization, as well as other eye inflammatory diseases, ocular tumors and diseases associated with choroidal or iris neovascularization. See, e.g., reviews by Waltman *et al.*, *Am. J. Ophthalm.* 85:704-710 (1978) and Gartner *et al.*, *Surv. Ophthalm.* 22:291-312 (1978).

Thus, within one aspect of the present invention methods are provided for treating  
30 neovascular diseases of the eye such as corneal neovascularization (including corneal graft neovascularization), comprising the step of administering to a patient a therapeutically effective amount of a compound (as described above) to the cornea, such that the formation

of blood vessels is inhibited. Briefly, the cornea is a tissue which normally lacks blood vessels. In certain pathological conditions however, capillaries may extend into the cornea from the pericorneal vascular plexus of the limbus. When the cornea becomes vascularized, it also becomes clouded, resulting in a decline in the patient's visual acuity. Visual loss may become complete if the cornea completely opacitates. A wide variety of disorders can result in corneal neovascularization, including for example, corneal infections (e.g., trachoma, herpes simplex keratitis, leishmaniasis and onchocerciasis), immunological processes (e.g., graft rejection and Stevens-Johnson's syndrome), alkali burns, trauma, inflammation (of any cause), toxic and nutritional deficiency states, and as a complication of wearing contact lenses.

Within particularly preferred embodiments of the invention, may be prepared for topical administration in saline (combined with any of the preservatives and antimicrobial agents commonly used in ocular preparations), and administered in eyedrop form. The solution or suspension may be prepared in its pure form and administered several times daily. Alternatively, anti-angiogenic compositions, prepared as described above, may also be administered directly to the cornea. Within preferred embodiments, the anti-angiogenic composition is prepared with a muco-adhesive polymer which binds to cornea. Within further embodiments, the anti-angiogenic factors or anti-angiogenic compositions may be utilized as an adjunct to conventional steroid therapy. Topical therapy may also be useful prophylactically in corneal lesions which are known to have a high probability of inducing an angiogenic response (such as chemical burns). In these instances the treatment, likely in combination with steroids, may be instituted immediately to help prevent subsequent complications.

Within other embodiments, the compounds described above may be injected directly into the corneal stroma by an ophthalmologist under microscopic guidance. The preferred site of injection may vary with the morphology of the individual lesion, but the goal of the administration would be to place the composition at the advancing front of the vasculature (i.e., interspersed between the blood vessels and the normal cornea). In most cases this would involve perilimbic corneal injection to "protect" the cornea from the advancing blood vessels. This method may also be utilized shortly after a corneal insult in order to prophylactically prevent corneal neovascularization. In this situation the material could be injected in the perilimbic cornea interspersed between the corneal lesion and its undesired

potential limbic blood supply. Such methods may also be utilized in a similar fashion to prevent capillary invasion of transplanted corneas. In a sustained-release form injections might only be required 2-3 times per year. A steroid could also be added to the injection solution to reduce inflammation resulting from the injection itself.

- 5           Within another aspect of the present invention, methods are provided for treating neovascular glaucoma, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. In one embodiment, the compound may be administered topically to the eye in order to treat early forms of neovascular glaucoma.
- 10       Within other embodiments, the compound may be implanted by injection into the region of the anterior chamber angle. Within other embodiments, the compound may also be placed in any location such that the compound is continuously released into the aqueous humor. Within another aspect of the present invention, methods are provided for treating proliferative diabetic retinopathy, comprising the step of administering to a patient a
- 15       therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eyes, such that the formation of blood vessels is inhibited.

          Within particularly preferred embodiments of the invention, proliferative diabetic retinopathy may be treated by injection into the aqueous humor or the vitreous, in order to increase the local concentration of the polynucleotide, polypeptide, antagonist and/or agonist

20       in the retina. Preferably, this treatment should be initiated prior to the acquisition of severe disease requiring photocoagulation.

          Within another aspect of the present invention, methods are provided for treating retrolental fibroplasia, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such

25       that the formation of blood vessels is inhibited. The compound may be administered topically, via intravitreal injection and/or via intraocular implants.

          Additionally, disorders which can be treated with the polynucleotides, polypeptides, agonists and/or antagonists include, but are not limited to, hemangioma, arthritis, psoriasis, angiofibroma, atherosclerotic plaques, delayed wound healing, granulations, hemophilic

30       joints, hypertrophic scars, nonunion fractures, Osler-Weber syndrome, pyogenic granuloma, scleroderma, trachoma, and vascular adhesions.

Moreover, disorders and/or states, which can be treated with the the polynucleotides, polypeptides, agonists and/or agonists include, but are not limited to, solid tumors, blood born tumors such as leukemias, tumor metastasis, Kaposi's sarcoma, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas, rheumatoid arthritis, psoriasis, ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, and uveitis, delayed wound healing, endometriosis, vasculogenesis, granulations, hypertrophic scars (keloids), nonunion fractures, scleroderma, trachoma, vascular adhesions, myocardial angiogenesis, coronary collaterals, cerebral collaterals, arteriovenous malformations, ischemic limb angiogenesis, Osler-Webber Syndrome, plaque neovascularization, telangiectasia, hemophilic joints, angiofibroma fibromuscular dysplasia, wound granulation, Crohn's disease, atherosclerosis, birth control agent by preventing vascularization required for embryo implantation controlling menstruation, diseases that have angiogenesis as a pathologic consequence such as cat scratch disease (Rochel minalia quintosa), ulcers (Helicobacter pylori), Bartonellosis and bacillary angiomatosis.

In one aspect of the birth control method, an amount of the compound sufficient to block embryo implantation is administered before or after intercourse and fertilization have occurred, thus providing an effective method of birth control, possibly a "morning after" method. Polynucleotides, polypeptides, agonists and/or agonists may also be used in controlling menstruation or administered as either a peritoneal lavage fluid or for peritoneal implantation in the treatment of endometriosis.

Polynucleotides, polypeptides, agonists and/or agonists of the present invention may be incorporated into surgical sutures in order to prevent stitch granulomas.

Polynucleotides, polypeptides, agonists and/or agonists may be utilized in a wide variety of surgical procedures. For example, within one aspect of the present invention a compositions (in the form of, for example, a spray or film) may be utilized to coat or spray an area prior to removal of a tumor, in order to isolate normal surrounding tissues from malignant tissue, and/or to prevent the spread of disease to surrounding tissues. Within other aspects of the present invention, compositions (e.g., in the form of a spray) may be delivered via endoscopic procedures in order to coat tumors, or inhibit angiogenesis in a desired locale. Within yet other aspects of the present invention, surgical meshes which have been coated

with anti- angiogenic compositions of the present invention may be utilized in any procedure wherein a surgical mesh might be utilized. For example, within one embodiment of the invention a surgical mesh laden with an anti-angiogenic composition may be utilized during abdominal cancer resection surgery (e.g., subsequent to colon resection) in order to provide support to the structure, and to release an amount of the anti-angiogenic factor.

Within further aspects of the present invention, methods are provided for treating tumor excision sites, comprising administering a polynucleotide, polypeptide, agonist and/or agonist to the resection margins of a tumor subsequent to excision, such that the local recurrence of cancer and the formation of new blood vessels at the site is inhibited. Within one embodiment of the invention, the anti-angiogenic compound is administered directly to the tumor excision site (e.g., applied by swabbing, brushing or otherwise coating the resection margins of the tumor with the anti-angiogenic compound). Alternatively, the anti-angiogenic compounds may be incorporated into known surgical pastes prior to administration. Within particularly preferred embodiments of the invention, the anti-angiogenic compounds are applied after hepatic resections for malignancy, and after neurosurgical operations.

Within one aspect of the present invention, polynucleotides, polypeptides, agonists and/or agonists may be administered to the resection margin of a wide variety of tumors, including for example, breast, colon, brain and hepatic tumors. For example, within one embodiment of the invention, anti-angiogenic compounds may be administered to the site of a neurological tumor subsequent to excision, such that the formation of new blood vessels at the site are inhibited.

The polynucleotides, polypeptides, agonists and/or agonists of the present invention may also be administered along with other anti-angiogenic factors. Representative examples of other anti-angiogenic factors include: Anti-Invasive Factor, retinoic acid and derivatives thereof, paclitaxel, Suramin, Tissue Inhibitor of Metalloproteinase-1, Tissue Inhibitor of Metalloproteinase-2, Plasminogen Activator Inhibitor-1, Plasminogen Activator Inhibitor-2, and various forms of the lighter "d group" transition metals.

Lighter "d group" transition metals include, for example, vanadium, molybdenum, tungsten, titanium, niobium, and tantalum species. Such transition metal species may form transition metal complexes. Suitable complexes of the above-mentioned transition metal species include oxo transition metal complexes.

Representative examples of vanadium complexes include oxo vanadium complexes such as vanadate and vanadyl complexes. Suitable vanadate complexes include metavanadate and orthovanadate complexes such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

Representative examples of tungsten and molybdenum complexes also include oxo complexes. Suitable oxo tungsten complexes include tungstate and tungsten oxide complexes. Suitable tungstate complexes include ammonium tungstate, calcium tungstate, sodium tungstate dihydrate, and tungstic acid. Suitable tungsten oxides include tungsten (IV) oxide and tungsten (VI) oxide. Suitable oxo molybdenum complexes include molybdate, molybdenum oxide, and molybdenyl complexes. Suitable molybdate complexes include ammonium molybdate and its hydrates, sodium molybdate and its hydrates, and potassium molybdate and its hydrates. Suitable molybdenum oxides include molybdenum (VI) oxide, molybdenum (VI) oxide, and molybdic acid. Suitable molybdenyl complexes include, for example, molybdenyl acetylacetonate. Other suitable tungsten and molybdenum complexes include hydroxo derivatives derived from, for example, glycerol, tartaric acid, and sugars.

A wide variety of other anti-angiogenic factors may also be utilized within the context of the present invention. Representative examples include platelet factor 4; protamine sulphate; sulphated chitin derivatives (prepared from queen crab shells), (Murata et al., Cancer Res. 51:22-26, 1991); Sulphated Polysaccharide Peptidoglycan Complex (SP- PG) (the function of this compound may be enhanced by the presence of steroids such as estrogen, and tamoxifen citrate); Staurosporine; modulators of matrix metabolism, including for example, proline analogs, cishydroxyproline, d,L-3,4-dehydroproline, Thiaproline, alpha,alpha-dipyridyl, aminopropionitrile fumarate; 4-propyl-5-(4-pyridinyl)-2(3H)-oxazolone; Methotrexate; Mitoxantrone; Heparin; Interferons; 2 Macroglobulin-serum; ChIMP-3 (Pavloff et al., J. Bio. Chem. 267:17321-17326, 1992); Chymostatin (Tomkinson et al., Biochem J. 286:475-480, 1992); Cyclodextrin Tetradecasulfate; Eponemycin; Camptothecin; Fumagillin (Ingber et al., Nature 348:555-557, 1990); Gold Sodium Thiomalate ("GST"; Matsubara and Ziff, J. Clin. Invest. 79:1440-1446, 1987); anticollagenase-serum; alpha2-antiplasmin (Holmes et al., J. Biol. Chem. 262(4):1659-1664, 1987); Bisantrone (National Cancer Institute); Lobenzarit disodium (N-(2)-carboxyphenyl-4-

chloroanthronilic acid disodium or "CCA"; Takeuchi et al., Agents Actions 36:312-316, 1992); Thalidomide; Angostatic steroid; AGM-1470; carboxynaminolmidazole; and metalloproteinase inhibitors such as BB94.

## 5 Diseases at the Cellular Level

Diseases associated with increased cell survival or the inhibition of apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as antagonists or agonists of the present invention, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and ovarian cancer); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection. In preferred embodiments, polynucleotides, polypeptides, and/or antagonists of the invention are used to inhibit growth, progression, and/or metasis of cancers, in particular those listed above.

Additional diseases or conditions associated with increased cell survival that could be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's



tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, 5 seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, 10 neuroblastoma, and retinoblastoma.

Diseases associated with increased apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, include AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Retinitis pigmentosa, Cerebellar degeneration and brain tumor 15 or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) myelodysplastic syndromes (such as aplastic anemia), graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion 20 injury), liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestosis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

#### **Wound Healing and Epithelial Cell Proliferation**

25 In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate epithelial cell proliferation and basal keratinocytes for the purpose of wound healing, and to stimulate hair follicle production and healing of dermal wounds. Polynucleotides or polypeptides, as well as 30 agonists or antagonists of the present invention, may be clinically useful in stimulating wound healing including surgical wounds, excisional wounds, deep wounds involving damage of the dermis and epidermis, eye tissue wounds, dental tissue wounds, oral cavity

wounds, diabetic ulcers, dermal ulcers, cubitus ulcers, arterial ulcers, venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and antineoplastic drugs and  
5 antimetabolites. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote dermal reestablishment subsequent to dermal loss

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to increase the adherence of skin grafts to a wound bed and to  
10 stimulate re-epithelialization from the wound bed. The following are types of grafts that polynucleotides or polypeptides, agonists or antagonists of the present invention, could be used to increase adherence to a wound bed: autografts, artificial skin, allografts, autodermic graft, autoepidermic grafts, avascular grafts, Blair-Brown grafts, bone graft, brephoplastic grafts, cutis graft, delayed graft, dermic graft, epidermic graft, fascia graft, full thickness  
15 graft, heterologous graft, xenograft, homologous graft, hyperplastic graft, lamellar graft, mesh graft, mucosal graft, Ollier-Thiersch graft, omentopial graft, patch graft, pedicle graft, penetrating graft, split skin graft, thick split graft. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, can be used to promote skin strength and to improve the appearance of aged skin.

20 It is believed that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, will also produce changes in hepatocyte proliferation, and epithelial cell proliferation in the lung, breast, pancreas, stomach, small intestine, and large intestine. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could promote proliferation of epithelial cells such as sebocytes, hair follicles; hepatocytes,  
25 type II pneumocytes, mucin-producing goblet cells, and other epithelial cells and their progenitors contained within the skin, lung, liver, and gastrointestinal tract. Polynucleotides or polypeptides, agonists or antagonists of the present invention, may promote proliferation of endothelial cells, keratinocytes, and basal keratinocytes.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present  
30 invention, could also be used to reduce the side effects of gut toxicity that result from radiation, chemotherapy treatments or viral infections. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may have a cytoprotective effect on

the small intestine mucosa. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may also stimulate healing of mucositis (mouth ulcers) that result from chemotherapy and viral infections.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could further be used in full regeneration of skin in full and partial thickness skin defects, including burns, (i.e., repopulation of hair follicles, sweat glands, and sebaceous glands), treatment of other skin defects such as psoriasis. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat epidermolysis bullosa, a defect in adherence of the epidermis to the underlying dermis which results in frequent, open and painful blisters by accelerating reepithelialization of these lesions. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to treat gastric and duodenal ulcers and help heal by scar formation of the mucosal lining and regeneration of glandular mucosa and duodenal mucosal lining more rapidly. Inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, are diseases which result in destruction of the mucosal surface of the small or large intestine, respectively. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote the resurfacing of the mucosal surface to aid more rapid healing and to prevent progression of inflammatory bowel disease. Treatment with polynucleotides or polypeptides, agonists or antagonists of the present invention, is expected to have a significant effect on the production of mucus throughout the gastrointestinal tract and could be used to protect the intestinal mucosa from injurious substances that are ingested or following surgery. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat diseases associated with the under expression.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to prevent and heal damage to the lungs due to various pathological states. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, which could stimulate proliferation and differentiation and promote the repair of alveoli and bronchiolar epithelium to prevent or treat acute or chronic lung damage. For example, emphysema, which results in the progressive loss of alveoli, and inhalation injuries, i.e., resulting from smoke inhalation and burns, that cause necrosis of the bronchiolar epithelium and alveoli could be effectively treated using polynucleotides or

polypeptides, agonists or antagonists of the present invention. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to stimulate the proliferation of and differentiation of type II pneumocytes, which may help treat or prevent disease such as hyaline membrane diseases, such as infant respiratory distress syndrome and bronchopulmonary dysplasia, in premature infants.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could stimulate the proliferation and differentiation of hepatocytes and, thus, could be used to alleviate or treat liver diseases and pathologies such as fulminant liver failure caused by cirrhosis, liver damage caused by viral hepatitis and toxic substances (i.e., acetaminophen, carbon tetrachloride and other hepatotoxins known in the art).

In addition, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat or prevent the onset of diabetes mellitus. In patients with newly diagnosed Types I and II diabetes, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to maintain the islet function so as to alleviate, delay or prevent permanent manifestation of the disease. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used as an auxiliary in islet cell transplantation to improve or promote islet cell function.

## **Neurological Diseases**

In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate neurological cell proliferation and/or differentiation. Therefore, polynucleotides, polypeptides, agonists and/or antagonists of the invention may be used to treat and/or detect neurologic diseases. Moreover, polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used as a marker or detector of a particular nervous system disease or disorder.

Examples of neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include brain diseases, such as metabolic brain diseases which includes phenylketonuria such as maternal phenylketonuria, pyruvate carboxylase deficiency, pyruvate dehydrogenase complex deficiency, Wernicke's Encephalopathy, brain edema, brain neoplasms such as

cerebellar neoplasms which include infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms, supratentorial neoplasms, canavan disease, cerebellar diseases such as cerebellar ataxia which include spinocerebellar degeneration such as ataxia telangiectasia, cerebellar dyssynergia, Friederich's Ataxia, Machado-Joseph Disease, olivopontocerebellar atrophy, cerebellar neoplasms such as infratentorial neoplasms, diffuse cerebral sclerosis such as encephalitis periaxialis, globoid cell leukodystrophy, metachromatic leukodystrophy and subacute sclerosing panencephalitis, cerebrovascular disorders (such as carotid artery diseases which include carotid artery thrombosis, carotid stenosis and Moyamoya Disease, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformations, cerebral artery diseases, cerebral embolism and thrombosis such as carotid artery thrombosis, sinus thrombosis and Wallenberg's Syndrome, cerebral hemorrhage such as epidural hematoma, subdural hematoma and subarachnoid hemorrhage, cerebral infarction, cerebral ischemia such as transient cerebral ischemia, Subclavian Steal Syndrome and vertebrobasilar insufficiency, vascular dementia such as multi-infarct dementia, periventricular leukomalacia, vascular headache such as cluster headache, migraine, dementia such as AIDS Dementia Complex, presenile dementia such as Alzheimer's Disease and Creutzfeldt-Jakob Syndrome, senile dementia such as Alzheimer's Disease and progressive supranuclear palsy, vascular dementia such as multi-infarct dementia, encephalitis which include encephalitis periaxialis, viral encephalitis such as epidemic encephalitis, Japanese Encephalitis, St. Louis Encephalitis, tick-borne encephalitis and West Nile Fever, acute disseminated encephalomyelitis, meningoencephalitis such as uveomeningoencephalitic syndrome, Postencephalitic Parkinson Disease and subacute sclerosing panencephalitis, encephalomalacia such as periventricular leukomalacia, epilepsy such as generalized epilepsy which includes infantile spasms, absence epilepsy, myoclonic epilepsy which includes MERRF Syndrome, tonic-clonic epilepsy, partial epilepsy such as complex partial epilepsy, frontal lobe epilepsy and temporal lobe epilepsy, post-traumatic epilepsy, status epilepticus such as Epilepsia Partialis Continua, Hallervorden-Spatz Syndrome, hydrocephalus such as Dandy-Walker Syndrome and normal pressure hydrocephalus, hypothalamic diseases such as hypothalamic neoplasms, cerebral malaria, narcolepsy which includes cataplexy, bulbar poliomyelitis, cerebri pseudotumor, Rett Syndrome, Reye's Syndrome, thalamic diseases, cerebral toxoplasmosis, intracranial tuberculoma and Zellweger Syndrome, central nervous

system infections such as AIDS Dementia Complex, Brain Abscess, subdural empyema, encephalomyelitis such as Equine Encephalomyelitis, Venezuelan Equine Encephalomyelitis, Necrotizing Hemorrhagic Encephalomyelitis, Visna, cerebral malaria, meningitis such as arachnoiditis, aseptic meningitis such as viral meningitis which includes lymphocytic choriomeningitis. Bacterial meningitis which includes Haemophilus Meningitis, Listeria Meningitis, Meningococcal Meningitis such as Waterhouse-Friderichsen Syndrome, Pneumococcal Meningitis and meningeal tuberculosis, fungal meningitis such as Cryptococcal Meningitis, subdural effusion, meningoencephalitis such as uvemeningoencephalitic syndrome, myelitis such as transverse myelitis, neurosyphilis such as tabes dorsalis, poliomyelitis which includes bulbar poliomyelitis and postpoliomyelitis syndrome, prion diseases (such as Creutzfeldt-Jakob Syndrome, Bovine Spongiform Encephalopathy, Gerstmann-Straussler Syndrome, Kuru, Scrapie) cerebral toxoplasmosis, central nervous system neoplasms such as brain neoplasms that include cerebellar neoplasms such as infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms and supratentorial neoplasms, meningeal neoplasms, spinal cord neoplasms which include epidural neoplasms, demyelinating diseases such as Canavan Diseases, diffuse cerebral sclerolysis which includes adrenoleukodystrophy, encephalitis periaxialis, globoid cell leukodystrophy, diffuse cerebral sclerosis such as metachromatic leukodystrophy, allergic encephalomyelitis, necrotizing hemorrhagic encephalomyelitis, progressive multifocal leukoencephalopathy, multiple sclerosis, central pontine myelinolysis, transverse myelitis, neuromyelitis optica, Scrapie, Swayback, Chronic Fatigue Syndrome, Visna, High Pressure Nervous Syndrome, Meningism, spinal cord diseases such as amyotonia congenita, amyotrophic lateral sclerosis, spinal muscular atrophy such as Werdnig-Hoffmann Disease, spinal cord compression, spinal cord neoplasms such as epidural neoplasms, syringomyelia, Tabes Dorsalis, Stiff-Man Syndrome, mental retardation such as Angelman Syndrome, Cri-du-Chat Syndrome, De Lange's Syndrome, Down Syndrome, Gangliosidoses such as gangliosidoses G(M1), Sandhoff Disease, Tay-Sachs Disease, Hartnup Disease, homocystinuria, Laurence-Moon- Biedl Syndrome, Lesch-Nyhan Syndrome, Maple Syrup Urine Disease, mucopolysaccharidosis such as fucosidosis, neuronal ceroid-lipofuscinosis, oculocerebrorenal syndrome, phenylketonuria such as maternal phenylketonuria, Prader-Willi Syndrome, Rett Syndrome, Rubinstein-Taybi Syndrome, Tuberous Sclerosis, WAGR Syndrome, nervous system abnormalities such as

holoprosencephaly, neural tube defects such as anencephaly which includes hydrangencephaly, Arnold-Chairi Deformity, encephalocele, meningocele, meningomyelocele, spinal dysraphism such as spina bifida cystica and spina bifida occulta, hereditary motor and sensory neuropathies which include Charcot-Marie Disease, Hereditary  
5 optic atrophy, Refsum's Disease, hereditary spastic paraplegia, Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies such as Congenital Analgesia and Familial Dysautonomia, Neurologic manifestations (such as agnosia that include Gerstmann's Syndrome, Amnesia such as retrograde amnesia, apraxia, neurogenic bladder, cataplexy, communicative disorders such as hearing disorders that includes deafness, partial hearing  
10 loss, loudness recruitment and tinnitus, language disorders such as aphasia which include agraphia, anomia, broca aphasia, and Wernicke Aphasia, Dyslexia such as Acquired Dyslexia, language development disorders, speech disorders such as aphasia which includes anomia, broca aphasia and Wernicke Aphasia, articulation disorders, communicative disorders such as speech disorders which include dysarthria, echolalia, mutism and stuttering,  
15 voice disorders such as aphonia and hoarseness, decerebrate state, delirium, fasciculation, hallucinations, meningism, movement disorders such as angelman syndrome, ataxia, athetosis, chorea, dystonia, hypokinesia, muscle hypotonia, myoclonus, tic, torticollis and tremor, muscle hypertonia such as muscle rigidity such as stiff-man syndrome, muscle spasticity, paralysis such as facial paralysis which includes Herpes Zoster Oticus,  
20 Gastroparesis, Hemiplegia, ophthalmoplegia such as diplopia, Duane's Syndrome, Horner's Syndrome, Chronic progressive external ophthalmoplegia such as Kearns Syndrome, Bulbar Paralysis, Tropical Spastic Paraparesis, Paraplegia such as Brown-Sequard Syndrome, quadriplegia, respiratory paralysis and vocal cord paralysis, paresis, phantom limb, taste disorders such as ageusia and dysgeusia, vision disorders such as amblyopia, blindness, color  
25 vision defects, diplopia, hemianopsia, scotoma and subnormal vision, sleep disorders such as hypersomnia which includes Kleine-Levin Syndrome, insomnia, and somnambulism, spasm such as trismus, unconsciousness such as coma, persistent vegetative state and syncope and vertigo, neuromuscular diseases such as amyotonia congenita, amyotrophic lateral sclerosis, Lambert-Eaton Myasthenic Syndrome, motor neuron disease, muscular atrophy such as  
30 spinal muscular atrophy, Charcot-Marie Disease and Werdnig-Hoffmann Disease, Postpoliomyelitis Syndrome, Muscular Dystrophy, Myasthenia Gravis, Myotonia Atrophica, Myotonia Confenita, Nemaline Myopathy, Familial Periodic Paralysis, Multiplex

Paramyoclonus, Tropical Spastic Paraparesis and Stiff-Man Syndrome, peripheral nervous system diseases such as acrodynia, amyloid neuropathies, autonomic nervous system diseases such as Adie's Syndrome, Barre-Lieou Syndrome, Familial Dysautonomia, Horner's Syndrome, Reflex Sympathetic Dystrophy and Shy-Drager Syndrome, Cranial Nerve Diseases such as Acoustic Nerve Diseases such as Acoustic Neuroma which includes Neurofibromatosis 2, Facial Nerve Diseases such as Facial Neuralgia, Melkersson-Rosenthal Syndrome, ocular motility disorders which includes amblyopia, nystagmus, oculomotor nerve paralysis, ophthalmoplegia such as Duane's Syndrome, Horner's Syndrome, Chronic Progressive External Ophthalmoplegia which includes Kearns Syndrome, Strabismus such as Esotropia and Exotropia, Oculomotor Nerve Paralysis, Optic Nerve Diseases such as Optic Atrophy which includes Hereditary Optic Atrophy, Optic Disk Drusen, Optic Neuritis such as Neuromyelitis Optica, Papilledema, Trigeminal Neuralgia, Vocal Cord Paralysis, Demyelinating Diseases such as Neuromyelitis Optica and Swayback, Diabetic neuropathies such as diabetic foot, nerve compression syndromes such as carpal tunnel syndrome, tarsal tunnel syndrome, thoracic outlet syndrome such as cervical rib syndrome, ulnar nerve compression syndrome, neuralgia such as causalgia, cervico-brachial neuralgia, facial neuralgia and trigeminal neuralgia, neuritis such as experimental allergic neuritis, optic neuritis, polyneuritis, polyradiculoneuritis and radiculitis such as polyradiculitis, hereditary motor and sensory neuropathies such as Charcot-Marie Disease, Hereditary Optic Atrophy, Refsum's Disease, Hereditary Spastic Paraplegia and Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies which include Congenital Analgesia and Familial Dysautonomia, POEMS Syndrome, Sciatica, Gustatory Sweating and Tetany).

### **Infectious Disease**

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.



Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention. Examples of viruses, include, but are not limited to Examples of viruses, include, but are not limited to the following DNA and RNA viruses and viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Dengue, EBV, HIV, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza A, Influenza B, and parainfluenza), Papiloma virus, Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiollitis, respiratory syncytial virus, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), Japanese B encephalitis, Junin, Chikungunya, Rift Valley fever, yellow fever, meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat: meningitis, Dengue, EBV, and/or hepatitis (e.g., hepatitis B). In an additional specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat patients nonresponsive to one or more other commercially available hepatitis vaccines. In a further specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat AIDS.

Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, include, but not limited to, the following Gram-Negative and Gram-positive bacteria and bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Cryptococcus neoformans, Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia

(e.g., *Borrelia burgdorferi*, Brucellosis, Candidiasis, *Campylobacter*, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, *E. coli* (e.g., Enterotoxigenic *E. coli* and Enterohemorrhagic *E. coli*), Enterobacteriaceae (*Klebsiella*, *Salmonella* (e.g., *Salmonella typhi*, and *Salmonella paratyphi*), *Serratia*, *Yersinia*), *Erysipelothrix*, *Helicobacter*,  
5 *Legionellosis*, *Leptospirosis*, *Listeria*, *Mycoplasmatales*, *Mycobacterium leprae*, *Vibrio cholerae*, *Neisseriaceae* (e.g., *Acinetobacter*, *Gonorrhea*, *Menigococcal*), *Meisseria meningitidis*, *Pasteurellacea* Infections (e.g., *Actinobacillus*, *Heamophilus* (e.g., *Heamophilus influenza type B*), *Pasteurella*), *Pseudomonas*, *Rickettsiaceae*, *Chlamydiaceae*, *Syphilis*, *Shigella* spp., *Staphylococcal*, *Meningiococcal*, *Pneumococcal* and *Streptococcal* (e.g.,  
10 *Streptococcus pneumoniae* and Group B *Streptococcus*). These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme  
15 Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, *Gonorrhea*, meningitis (e.g., meningitis types A and B), *Chlamydia*, *Syphilis*, *Diphtheria*, *Leprosy*, *Paratuberculosis*, *Tuberculosis*, *Lupus*, *Botulism*, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections.  
20 Polynucleotides or polypeptides, agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, Polynucleotides, polypeptides, agonists or antagonists of the invention are used to treat: tetanus, *Diphtheria*, botulism, and/or meningitis type B.

Moreover, parasitic agents causing disease or symptoms that can be treated or  
25 detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, the following families or class: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and *Trichomonas* and Sporozoans (e.g., *Plasmodium virax*, *Plasmodium falciparum*,  
30 *Plasmodium malariae* and *Plasmodium ovale*). These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic

infections (e.g., AIDS related), malaria, pregnancy complications, and toxoplasmosis. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

### **Regeneration**

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vasculature (including vascular and lymphatics), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotides or polypeptides, as well as agonists or antagonists of the present invention.

### **Chemotaxis**

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may have chemotaxis activity. A chemotactic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may increase chemotactic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotactic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could be used as an inhibitor of chemotaxis.

### **Binding Activity**

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit (antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules  
5 include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide  
10 binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the  
15 expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled  
20 competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound  
25 with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the  
30 polypeptide or by competing with the polypeptide for a substrate.

Additionally, the receptor to which the polypeptide of the present invention binds can be identified by numerous methods known to those of skill in the art, for example, ligand

panning and FACS sorting (Coligan, et al., Current Protocols in Immun., 1(2), Chapter 5, (1991)). For example, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the polypeptides, for example, NIH3T3 cells which are known to contain multiple receptors for the FGF family proteins, and SC-3 cells, and a  
5 cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the polypeptides. Transfected cells which are grown on glass slides are exposed to the polypeptide of the present invention, after they have been labelled. The polypeptides can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase.

10 Following fixation and incubation, the slides are subjected to auto-radiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an iterative sub-pooling and re-screening process, eventually yielding a single clones that encodes the putative receptor.

As an alternative approach for receptor identification, the labeled polypeptides can be  
15 photoaffinity linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE analysis and exposed to X-ray film. The labeled complex containing the receptors of the polypeptides can be excised, resolved into peptide fragments, and subjected to protein microsequencing. The amino acid sequence obtained from microsequencing would be used to design a set of degenerate oligonucleotide  
20 probes to screen a cDNA library to identify the genes encoding the putative receptors.

Moreover, the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling") may be employed to modulate the activities of the polypeptide of the present invention thereby effectively generating agonists and antagonists of the polypeptide of the present invention. *See generally*, U.S.  
25 Patent Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458, and Patten, P. A., *et al.*, *Curr. Opinion Biotechnol.* 8:724-33 (1997); Harayama, S. *Trends Biotechnol.* 16(2):76-82 (1998); Hansson, L. O., *et al.*, *J. Mol. Biol.* 287:265-76 (1999); and Lorenzo, M. M. and Blasco, R. *Biotechniques* 24(2):308-13 (1998) (each of these patents and publications are hereby incorporated by reference). In one embodiment, alteration of polynucleotides and  
30 corresponding polypeptides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments into a desired molecule by homologous, or site-specific, recombination. In another embodiment, polynucleotides and corresponding

polypeptides may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of the polypeptide of the present invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules. In preferred embodiments, the heterologous molecules are family members. In further preferred embodiments, the heterologous molecule is a growth factor such as, for example, platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I), transforming growth factor (TGF)-alpha, epidermal growth factor (EGF), fibroblast growth factor (FGF), TGF-beta, bone morphogenetic protein (BMP)-2, BMP-4, BMP-5, BMP-6, BMP-7, activins A and B, decapentaplegic(dpp), 60A, OP-2, dorsalin, growth differentiation factors (GDFs), nodal, MIS, inhibin-alpha, TGF-beta1, TGF-beta2, TGF-beta3, TGF-beta5, and glial-derived neurotrophic factor (GDNF).

Other preferred fragments are biologically active fragments of the polypeptide of the present invention. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Additionally, this invention provides a method of screening compounds to identify those which modulate the action of the polypeptide of the present invention. An example of such an assay comprises combining a mammalian fibroblast cell, a the polypeptide of the present invention, the compound to be screened and  $^3\text{[H]}$  thymidine under cell culture conditions where the fibroblast cell would normally proliferate. A control assay may be performed in the absence of the compound to be screened and compared to the amount of fibroblast proliferation in the presence of the compound to determine if the compound stimulates proliferation by determining the uptake of  $^3\text{[H]}$  thymidine in each case. The amount of fibroblast cell proliferation is measured by liquid scintillation chromatography which measures the incorporation of  $^3\text{[H]}$  thymidine. Both agonist and antagonist compounds may be identified by this procedure.

In another method, a mammalian cell or membrane preparation expressing a receptor for a polypeptide of the present invention is incubated with a labeled polypeptide of the

present invention in the presence of the compound. The ability of the compound to enhance or block this interaction could then be measured. Alternatively, the response of a known second messenger system following interaction of a compound to be screened and the receptor is measured and the ability of the compound to bind to the receptor and elicit a second messenger response is measured to determine if the compound is a potential agonist or antagonist. Such second messenger systems include but are not limited to, cAMP guanylate cyclase, ion channels or phosphoinositide hydrolysis.

All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptides of the invention from suitably manipulated cells or tissues.

Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the present invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the present invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

### **Targeted Delivery**

In another embodiment, the invention provides a method of delivering compositions to targeted cells expressing a receptor for a polypeptide of the invention, or cells expressing a cell bound form of a polypeptide of the invention.

As discussed herein, polypeptides or antibodies of the invention may be associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (including antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method



for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

5 In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention (e.g., polypeptides of the invention or antibodies of the invention) in association with toxins or cytotoxic prodrugs.

By "toxin" is meant compounds that bind and activate endogenous cytotoxic effector  
10 systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an  
15 inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNase, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. By "cytotoxic prodrug" is meant a non-toxic compound that is converted by an enzyme, normally present in the cell, into a cytotoxic compound. Cytotoxic prodrugs that may be  
20 used according to the methods of the invention include, but are not limited to, glutamyl derivatives of benzoic acid mustard alkylating agent, phosphate derivatives of etoposide or mitomycin C, cytosine arabinoside, daunorubisin, and phenoxyacetamide derivatives of doxorubicin.

## 25 Drug Screening

Further contemplated is the use of the polypeptides of the present invention, or the polynucleotides encoding these polypeptides, to screen for molecules which modify the activities of the polypeptides of the present invention. Such a method would include contacting the polypeptide of the present invention with a selected compound(s) suspected of  
30 having antagonist or agonist activity, and assaying the activity of these polypeptides following binding.

This invention is particularly useful for screening therapeutic compounds by using the

polypeptides of the present invention, or binding fragments thereof, in any of a variety of drug screening techniques. The polypeptide or fragment employed in such a test may be affixed to a solid support, expressed on a cell surface, free in solution, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells  
5 which are stably transformed with recombinant nucleic acids expressing the polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. One may measure, for example, the formulation of complexes between the agent being tested and a polypeptide of the present invention.

Thus, the present invention provides methods of screening for drugs or any other  
10 agents which affect activities mediated by the polypeptides of the present invention. These methods comprise contacting such an agent with a polypeptide of the present invention or a fragment thereof and assaying for the presence of a complex between the agent and the polypeptide or a fragment thereof, by methods well known in the art. In such a competitive binding assay, the agents to screen are typically labeled. Following incubation, free agent is  
15 separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of a particular agent to bind to the polypeptides of the present invention.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to the polypeptides of the present invention, and  
20 is described in great detail in European Patent Application 84/03564, published on September 13, 1984, which is incorporated herein by reference herein. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with polypeptides of the present invention and washed. Bound polypeptides are then detected by methods well known  
25 in the art. Purified polypeptides are coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies may be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding polypeptides of the present invention  
30 specifically compete with a test compound for binding to the polypeptides or fragments thereof. In this manner, the antibodies are used to detect the presence of any peptide which shares one or more antigenic epitopes with a polypeptide of the invention.

**Antisense And Ribozyme (Antagonists)**

In specific embodiments, antagonists according to the present invention are nucleic acids corresponding to the sequences contained in SEQ ID NO:X, or the complementary strand thereof, and/or to nucleotide sequences contained in the cDNA contained in the related cDNA clone identified in Table 1. In one embodiment, antisense sequence is generated internally, by the organism, in another embodiment, the antisense sequence is separately administered (see, for example, O'Connor, J., Neurochem. 56:560 (1991). Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Antisense technology can be used to control gene expression through antisense DNA or RNA, or through triple-helix formation. Antisense techniques are discussed for example, in Okano, J., Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance, Lee et al., Nucleic Acids Research 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1300 (1991). The methods are based on binding of a polynucleotide to a complementary DNA or RNA.

For example, the use of c-myc and c-myb antisense RNA constructs to inhibit the growth of the non-lymphocytic leukemia cell line HL-60 and other cell lines was previously described. (Wickstrom et al. (1988); Anfossi et al. (1989)). These experiments were performed in vitro by incubating cells with the oligoribonucleotide. A similar procedure for in vivo use is described in WO 91/15580. Briefly, a pair of oligonucleotides for a given antisense RNA is produced as follows: A sequence complimentary to the first 15 bases of the open reading frame is flanked by an EcoRI site on the 5' end and a HindIII site on the 3' end. Next, the pair of oligonucleotides is heated at 90°C for one minute and then annealed in 2X ligation buffer (20mM TRIS HCl pH 7.5, 10mM MgCl<sub>2</sub>, 10mM dithiothreitol (DTT) and 0.2 mM ATP) and then ligated to the EcoRI/Hind III site of the retroviral vector PMV7 (WO 91/15580).

For example, the 5' coding portion of a polynucleotide that encodes the polypeptide of the present invention may be used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription thereby preventing transcription and the

production of the receptor. The antisense RNA oligonucleotide hybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into receptor polypeptide.

In one embodiment, the antisense nucleic acid of the invention is produced intracellularly by transcription from an exogenous sequence. For example, a vector or a portion thereof, is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the antisense nucleic acid. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art, used for replication and expression in vertebrate cells. Expression of the sequence encoding the polypeptide of the present invention or fragments thereof, can be by any promoter known in the art to act in vertebrate, preferably human cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, *Nature* 29:304-310 (1981)), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., *Cell* 22:787-797 (1980)), the herpes thymidine promoter (Wagner et al., *Proc. Natl. Acad. Sci. U.S.A.* 78:1441-1445 (1981)), the regulatory sequences of the metallothionein gene (Brinster, et al., *Nature* 296:39-42 (1982)), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a gene of the present invention. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the larger the hybridizing nucleic acid, the more base mismatches with a RNA it may contain and still form a stable duplex (or triplex as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

Oligonucleotides that are complementary to the 5' end of the message, e.g., the 5' untranslated sequence up to and including the AUG initiation codon, should work most

efficiently at inhibiting translation. However, sequences complementary to the 3' untranslated sequences of mRNAs have been shown to be effective at inhibiting translation of mRNAs as well. See generally, Wagner, R., 1994, *Nature* 372:333-335. Thus, oligonucleotides complementary to either the 5'- or 3'- non- translated, non-coding regions of polynucleotide sequences described herein could be used in an antisense approach to inhibit translation of endogenous mRNA. Oligonucleotides complementary to the 5' untranslated region of the mRNA should include the complement of the AUG start codon. Antisense oligonucleotides complementary to mRNA coding regions are less efficient inhibitors of translation but could be used in accordance with the invention. Whether designed to hybridize to the 5'-, 3'- or coding region of mRNA of the present invention, antisense nucleic acids should be at least six nucleotides in length, and are preferably oligonucleotides ranging from 6 to about 50 nucleotides in length. In specific aspects the oligonucleotide is at least 10 nucleotides, at least 17 nucleotides, at least 25 nucleotides or at least 50 nucleotides.

The polynucleotides of the invention can be DNA or RNA or chimeric mixtures or derivatives or modified versions thereof, single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone, for example, to improve stability of the molecule, hybridization, etc. The oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors in vivo), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre et al., 1987, *Proc. Natl. Acad. Sci.* 84:648-652; PCT Publication No. WO88/09810, published December 15, 1988) or the blood-brain barrier (see, e.g., PCT Publication No. WO89/10134, published April 25, 1988), hybridization-triggered cleavage agents. (See, e.g., Krol et al., 1988, *BioTechniques* 6:958-976) or intercalating agents. (See, e.g., Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

The antisense oligonucleotide may comprise at least one modified base moiety which is selected from the group including, but not limited to, 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine,

2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

The antisense oligonucleotide may also comprise at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the antisense oligonucleotide comprises at least one modified phosphate backbone selected from the group including, but not limited to, a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal or analog thereof.

In yet another embodiment, the antisense oligonucleotide is an a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual b-units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641). The oligonucleotide is a 2'-O-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analogue (Inoue et al., 1987, FEBS Lett. 215:327-330).

Polynucleotides of the invention may be synthesized by standard methods known in the art, e.g. by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligonucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. U.S.A. 85:7448-7451), etc.

While antisense nucleotides complementary to the coding region sequence could be used, those complementary to the transcribed untranslated region are most preferred.

Potential antagonists according to the invention also include catalytic RNA, or a ribozyme (See, e.g., PCT International Publication WO 90/11364, published October 4, 1990; Sarver et al, Science 247:1222-1225 (1990). While ribozymes that cleave mRNA at

site specific recognition sequences can be used to destroy mRNAs, the use of hammerhead ribozymes is preferred. Hammerhead ribozymes cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The sole requirement is that the target mRNA have the following sequence of two bases: 5'-UG-3'.

5 The construction and production of hammerhead ribozymes is well known in the art and is described more fully in Haseloff and Gerlach, Nature 334:585-591 (1988). There are numerous potential hammerhead ribozyme cleavage sites within the nucleotide sequence of SEQ ID NO:X. Preferably, the ribozyme is engineered so that the cleavage recognition site is located near the 5' end of the mRNA; i.e., to increase efficiency and minimize the  
10 intracellular accumulation of non-functional mRNA transcripts.

As in the antisense approach, the ribozymes of the invention can be composed of modified oligonucleotides (e.g. for improved stability, targeting, etc.) and should be delivered to cells which express in vivo. DNA constructs encoding the ribozyme may be introduced into the cell in the same manner as described above for the introduction of antisense encoding  
15 DNA. A preferred method of delivery involves using a DNA construct "encoding" the ribozyme under the control of a strong constitutive promoter, such as, for example, pol III or pol II promoter, so that transfected cells will produce sufficient quantities of the ribozyme to destroy endogenous messages and inhibit translation. Since ribozymes unlike antisense molecules, are catalytic, a lower intracellular concentration is required for efficiency.

20 Antagonist/agonist compounds may be employed to inhibit the cell growth and proliferation effects of the polypeptides of the present invention on neoplastic cells and tissues, i.e. stimulation of angiogenesis of tumors, and, therefore, retard or prevent abnormal cellular growth and proliferation, for example, in tumor formation or growth.

The antagonist/agonist may also be employed to prevent hyper-vascular diseases, and  
25 prevent the proliferation of epithelial lens cells after extracapsular cataract surgery. Prevention of the mitogenic activity of the polypeptides of the present invention may also be desirous in cases such as restenosis after balloon angioplasty.

The antagonist/agonist may also be employed to prevent the growth of scar tissue during wound healing.

30 The antagonist/agonist may also be employed to treat the diseases described herein.

Thus, the invention provides a method of treating disorders or diseases, including but not limited to the disorders or diseases listed throughout this application, associated with

overexpression of a polynucleotide of the present invention by administering to a patient (a) an antisense molecule directed to the polynucleotide of the present invention, and/or (b) a ribozyme directed to the polynucleotide of the present invention.

## 5 **Other Activities**

A polypeptide, polynucleotide, agonist, or antagonist of the present invention, as a result of the ability to stimulate vascular endothelial cell growth, may be employed in treatment for stimulating re-vascularization of ischemic tissues due to various disease conditions such as thrombosis, arteriosclerosis, and other cardiovascular conditions. The  
10 polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to stimulate angiogenesis and limb regeneration, as discussed above.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for treating wounds due to injuries, burns, post-operative tissue repair, and ulcers since they are mitogenic to various cells of different origins, such as fibroblast cells  
15 and skeletal muscle cells, and therefore, facilitate the repair or replacement of damaged or diseased tissue.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed stimulate neuronal growth and to treat and prevent neuronal damage which occurs in certain neuronal disorders or neuro-degenerative conditions such as Alzheimer's  
20 disease, Parkinson's disease, and AIDS-related complex. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may have the ability to stimulate chondrocyte growth, therefore, they may be employed to enhance bone and periodontal regeneration and aid in tissue transplants or bone grafts.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be  
25 also be employed to prevent skin aging due to sunburn by stimulating keratinocyte growth.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for preventing hair loss, since FGF family members activate hair-forming cells and promotes melanocyte growth. Along the same lines, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be employed to stimulate growth and  
30 differentiation of hematopoietic cells and bone marrow cells when used in combination with other cytokines.



A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to maintain organs before transplantation or for supporting cell culture of primary tissues. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for inducing tissue of mesodermal origin to differentiate in early embryos.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, circadian rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

The above-recited applications have uses in a wide variety of hosts. Such hosts include, but are not limited to, human, murine, rabbit, goat, guinea pig, camel, horse, mouse, rat, hamster, pig, micro-pig, chicken, goat, cow, sheep, dog, cat, non-human primate, and human. In specific embodiments, the host is a mouse, rabbit, goat, guinea pig, chicken, rat, hamster, pig, sheep, dog or cat. In preferred embodiments, the host is a mammal. In most preferred embodiments, the host is a human.

#### **Other Preferred Embodiments**

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which comprises a cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least  
5 50 contiguous nucleotides is included in the nucleotide sequence of an open reading frame sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the  
10 deposit.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

15 A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a  
20 sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and  
25 determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected  
30 from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a

nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleotide sequence of SEQ ID NO:X; or the cDNA in the related cDNA clone identified in Table 1 which encodes a protein, wherein the method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence of the cDNA in the related cDNA clone contained in the deposit.

Also preferred is the above method for diagnosing a pathological condition which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the

group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

5 Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a DNA microarray or "chip" of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, 50, 100, 150, 200, 250, 300, 500, 1000, 2000, 3000 or 4000 nucleotide sequences, wherein at least one sequence in said DNA microarray or "chip" is at least 95% identical to a sequence of at least 50 contiguous  
10 nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the cDNA clone referenced in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least  
15 90% identical to a sequence of at least about 10 contiguous amino acids in the polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid  
20 sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a  
25 polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

30 Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a portion of said polypeptide encoded by the cDNA clone referenced in Table 1; a polypeptide encoded by SEQ ID NO:X; and/or the polypeptide sequence of SEQ ID NO:Y.

5 Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid  
10 sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Further preferred is an isolated antibody which binds specifically to a polypeptide  
15 comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is a method for detecting in a biological sample a polypeptide  
20 comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule  
25 in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from  
30 said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in

a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleic acid sequence identified in Table 1 encoding a polypeptide, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of:

polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a  
5 prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

10 Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

15 Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a human protein comprising an amino acid sequence selected from the group consisting of:  
20 polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a protein activity, which method comprises administering to such an individual a  
25 Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to increase the level of said protein activity in said individual.

Also preferred is a method of treatment of an individual in need of a decreased level of a protein activity, which method comprised administering to such an individual a  
30 Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to decrease the level of said protein activity in said individual.



Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

*Examples**Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample*

5 Each deposited cDNA clone is contained in a plasmid vector. Table 5 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The following correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a  
 10 particular clone is identified in Table 5 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

	<u>Vector Used to Construct Library</u>	<u>Corresponding Deposited Plasmid</u>
	Lambda Zap	pBluescript (pBS)
	Uni-Zap XR	pBluescript (pBS)
15	Zap Express	pBK
	lalfmid BA	plafmid BA
	pSport1	pSport1
	pCMVSPORT 2.0	pCMVSPORT 2.0
	pCMVSPORT 3.0	pCMVSPORT 3.0
20	pCR <sup>®</sup> 2.1	pCR <sup>®</sup> 2.1

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 25 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS. The S and K refers to the orientation of the polylinker to the T7 and T3  
 30

primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the fl origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the fl ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lacmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR<sup>®</sup>2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 5, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited by reference to Table 2 and 5 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone referenced in Table 1.

**TABLE 5**

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HUKA HUKB HUKC HUKD HUKF HUKG	Human Uterine Cancer	Lambda ZAP II	LP01
HCNA HCNB	Human Colon	Lambda Zap II	LP01
HFFA	Human Fetal Brain, random primed	Lambda Zap II	LP01
HTWA	Resting T-Cell	Lambda ZAP II	LP01
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP01
HLMB HLMF HLMG HLMH HLMI HLMJ HLMM HLMN	breast lymph node CDNA library	Lambda ZAP II	LP01
HCQA HCQB	human colon cancer	Lambda ZAP II	LP01
HMEA HMEC HMED HMEE HMEF HMEG HMEI HMEJ HMEK HMEI	Human Microvascular Endothelial Cells, fract. A	Lambda ZAP II	LP01
HUSA HUSC	Human Umbilical Vein Endothelial Cells, fract. A	Lambda ZAP II	LP01
HLQA HLQB	Hepatocellular Tumor	Lambda ZAP II	LP01
HHGA HHGB HHGC HHGD	Hemangiopericytoma	Lambda ZAP II	LP01
HSDM	Human Striatum Depression, re-rescue	Lambda ZAP II	LP01
HUSH	H Umbilical Vein Endothelial Cells, fract. A, re-excision	Lambda ZAP II	LP01
HSGS	Salivary gland, subtracted	Lambda ZAP II	LP01
HFXA HFXB HFXC HFXD HFXE HFXF HFXG HFXH	Brain frontal cortex	Lambda ZAP II	LP01
HPQA HPQB HPQC	PERM TF274	Lambda ZAP II	LP01
HFXJ HFXK	Brain Frontal Cortex, re-excision	Lambda ZAP II	LP01
HCWA HCWB HCWC HCWD HCWE HCWF HCWG HCWH HCWI HCWJ HCWK	CD34 positive cells (Cord Blood)	ZAP Express	LP02
HCUA HCUB HCUC	CD34 depleted Buffy Coat (Cord Blood)	ZAP Express	LP02
HRSM	A-14 cell line	ZAP Express	LP02
HRSA	A1-CELL LINE	ZAP Express	LP02
HCUD HCUE HCUF HCUG HCUH HCUI	CD34 depleted Buffy Coat (Cord Blood), re-excision	ZAP Express	LP02
HBXE HBXF HBXG	H. Whole Brain #2, re-excision	ZAP Express	LP02
HRLM	L8 cell line	ZAP Express	LP02
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP02
HUDA HUDB HUDC	Testes	ZAP Express	LP02
HHTM HHTN HHTO	H. hypothalamus, fract. A; re-excision	ZAP Express	LP02
HHTL	H. hypothalamus, fract. A	ZAP Express	LP02
HASA HASD	Human Adult Spleen	Uni-ZAP XR	LP03
HFKC HFKD HFKE HFKF HFKG	Human Fetal Kidney	Uni-ZAP XR	LP03
HE8A HE8B HE8C HE8D HE8E HE8F HE8M HE8N	Human 8 Week Whole Embryo	Uni-ZAP XR	LP03
HGBA HGBD HGBE HGBF HGBG HGBH HGBI	Human Gall Bladder	Uni-ZAP XR	LP03
HLHA HLHB HLHC HLHD HLHE HLHF HLHG HLHH HLHQ	Human Fetal Lung III	Uni-ZAP XR	LP03
HPMA HPMB HPMC HPMD HPME HPMF HPMG HPMH	Human Placenta	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP03
HSIA HSIC HSID HSIE	Human Adult Small Intestine	Uni-ZAP XR	LP03
HTEA HTEB HTEC HTED HTEE HTEF HTEG HTEH HTEI HTEJ HTEK	Human Testes	Uni-ZAP XR	LP03
HTPA HTPB HTPC HTPD HTPE	Human Pancreas Tumor	Uni-ZAP XR	LP03
HTTA HTTB HTTC HTTD HTTE HTTF	Human Testes Tumor	Uni-ZAP XR	LP03
HAPA HAPB HAPC HAPM	Human Adult Pulmonary	Uni-ZAP XR	LP03
HETA HETB HETC HETD HETE HETF HETG HETH HETI	Human Endometrial Tumor	Uni-ZAP XR	LP03
HHFB HHFC HHFD HHFE HHFF HHFG HHFH HHFI	Human Fetal Heart	Uni-ZAP XR	LP03
HHPB HHPC HHPD HHPE HHPF HHPG HHPH	Human Hippocampus	Uni-ZAP XR	LP03
HCE1 HCE2 HCE3 HCE4 HCE5 HCEB HCEC HCED HCEE HCEF HCEG	Human Cerebellum	Uni-ZAP XR	LP03
HUVB HUV C HUVD HUVE	Human Umbilical Vein, Endo. remake	Uni-ZAP XR	LP03
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP03
HTAA HTAB HTAC HTAD HTAE	Human Activated T-Cells	Uni-ZAP XR	LP03
HFEA HFEB HFEC	Human Fetal Epithelium (Skin)	Uni-ZAP XR	LP03
HJPA HJPB HJPC HJPD	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Uni-ZAP XR	LP03
HESA	Human epithelioid sarcoma	Uni-Zap XR	LP03
HLTA HLTB HLTC HLTD HLTE HLTF	Human T-Cell Lymphoma	Uni-ZAP XR	LP03
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP03
HRDA HRDB HRDC HRDD HRDE HRDF	Human Rhabdomyosarcoma	Uni-ZAP XR	LP03
HCAA HCAB HCAC	Cem cells cyclohexamide treated	Uni-ZAP XR	LP03
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HSUA HSUB HSUC HSUM	Supt Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HT4A HT4C HT4D	Activated T-Cells, 12 hrs.	Uni-ZAP XR	LP03
HE9A HE9B HE9C HE9D HE9E HE9F HE9G HE9H HE9M HE9N	Nine Week Old Early Stage Human	Uni-ZAP XR	LP03
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP03
HT5A	Activated T-Cells, 24 hrs.	Uni-ZAP XR	LP03
HFGA HFGM	Human Fetal Brain	Uni-ZAP XR	LP03
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP03
HBGB HBGD	Human Primary Breast Cancer	Uni-ZAP XR	LP03
HBNA HBNB	Human Normal Breast	Uni-ZAP XR	LP03
HCAS	Cem Cells, cyclohexamide treated, subtra	Uni-ZAP XR	LP03
HHPS	Human Hippocampus, subtracted	pBS	LP03
HKCS HKCU	Human Colon Cancer, subtracted	pBS	LP03
HRGS	Raji cells, cyclohexamide treated, subtracted	pBS	LP03
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBS	LP03
HT4S	Activated T-Cells, 12 hrs, subtracted	Uni-ZAP XR	LP03
HCDA HCDB HCDC HCDD HCDE	Human Chondrosarcoma	Uni-ZAP XR	LP03
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP03
HTLA HTLB HTLC HTLD HTLE	Human adult testis, large inserts	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HTLF			
HLMA HLMC HLMD	Breast Lymph node cDNA library	Uni-ZAP XR	LP03
H6EA H6EB H6EC	HL-60, PMA 4H	Uni-ZAP XR	LP03
HTXA HTXB HTXC HTXD HTXE HTXF HTXG HTXH	Activated T-Cell (12hs)/Thiouridine labelledEco	Uni-ZAP XR	LP03
HNFA HNFH HNFC HNFD HNFE HNFF HNFG HNFH HNFJ	Human Neutrophil, Activated	Uni-ZAP XR	LP03
HTOB HTOC	HUMAN TONSILS, FRACTION 2	Uni-ZAP XR	LP03
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP03
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP03
HORB	Human OB HOS treated (10 nM E2) fraction I	Uni-ZAP XR	LP03
HSVA HSVB HSVC	Human Chronic Synovitis	Uni-ZAP XR	LP03
HROA	HUMAN STOMACH	Uni-ZAP XR	LP03
HBJA HBJB HBJC HBJD HBJE HBJF HBJG HBJH HBJI HBJJ HBJK	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP03
HCRA HCRB HCRC	human corpus colosum	Uni-ZAP XR	LP03
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP03
HDSA	Dermatofibrosarcoma Protuberance	Uni-ZAP XR	LP03
HMWA HMWB HMWC HMWD HMWE HMWF HMWG HMWH HMWI HMWJ	Bone Marrow Cell Line (RS4;11)	Uni-ZAP XR	LP03
HSOA	stomach cancer (human)	Uni-ZAP XR	LP03
HERA	SKIN	Uni-ZAP XR	LP03
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP03
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP03
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP03
HBCA HBCB	H. Lymph node breast Cancer	Uni-ZAP XR	LP03
HPWT	Human Prostate BPH, re-excision	Uni-ZAP XR	LP03
HFVG HFVH HFVI	Fetal Liver, subtraction II	pBS	LP03
HNFI	Human Neutrophils, Activated, re- excision	pBS	LP03
HBMB HBMC HBMD	Human Bone Marrow, re-excision	pBS	LP03
HKML HKMM HKMN	H. Kidney Medulla, re-excision	pBS	LP03
HKIX HKIY	H. Kidney Cortex, subtracted	pBS	LP03
HADT	H. Amygdala Depression, subtracted	pBS	LP03
H6AS	HL-60, untreated, subtracted	Uni-ZAP XR	LP03
H6ES	HL-60, PMA 4H, subtracted	Uni-ZAP XR	LP03
H6BS	HL-60, RA 4h, Subtracted	Uni-ZAP XR	LP03
H6CS	HL-60, PMA 1d, subtracted	Uni-ZAP XR	LP03
HTXJ HTXK	Activated T-cell(12h)/Thiouridine-re- excision	Uni-ZAP XR	LP03
HMSA HMSB HMSC HMSE HMSE HMSF HMSG HMSH HMSI HMSJ HMSK	Monocyte activated	Uni-ZAP XR	LP03
HAGA HAGB HAGC HAGD HAGE HAGF	Human Amygdala	Uni-ZAP XR	LP03
HSRA HSRB HSRE	STROMAL -OSTEOCLASTOMA	Uni-ZAP XR	LP03
HSRD HSRF HSRG HSRH	Human Osteoclastoma Stromal Cells - unamplified	Uni-ZAP XR	LP03
HSQA HSQB HSQC HSQD HSQE	Stromal cell TF274	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HSQF HSQG			
HSKA HSKB HSKC HSKD HSKE HSKF HSKZ	Smooth muscle, serum treated	Uni-ZAP XR	LP03
HSLA HSLB HSLC HSLD HSLE HSLF HSLG	Smooth muscle, control	Uni-ZAP XR	LP03
HSDA HSDD HSDE HSDF HSDG HSDH	Spinal cord	Uni-ZAP XR	LP03
HPWS	Prostate-BPH subtracted II	pBS	LP03
HSKW HSKX HSKY	Smooth Muscle- HASTE normalized	pBS	LP03
HFPB HFPC HFPD	H. Frontal cortex, epileptic; re-excision	Uni-ZAP XR	LP03
HSDI HSDJ HSDK	Spinal Cord, re-excision	Uni-ZAP XR	LP03
HSKN HSKO	Smooth Muscle Serum Treated, Norm	pBS	LP03
HSKG HSKH HSKI	Smooth muscle, serum induced, re-exc	pBS	LP03
HFCA HFCB HFCC HFCD HFCE HFCF	Human Fetal Brain	Uni-ZAP XR	LP04
HPTA HPTB HPTD	Human Pituitary	Uni-ZAP XR	LP04
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP04
HE6B HE6C HE6D HE6E HE6F HE6G HE6S	Human Whole Six Week Old Embryo	Uni-ZAP XR	LP04
HSSA HSSB HSSC HSSD HSSE HSSF HSSG HSSH HSSI HSSJ HSSK HE7T	Human Synovial Sarcoma	Uni-ZAP XR	LP04
HEPA HEPB HEPD	7 Week Old Early Stage Human, subtracted	Uni-ZAP XR	LP04
HEPA HEPB HEPD	Human Epididymus	Uni-ZAP XR	LP04
HSNA HSNB HSNB HSNM HSNM	Human Synovium	Uni-ZAP XR	LP04
HPFB HPFC HPFD HPFE	Human Prostate Cancer, Stage C fraction	Uni-ZAP XR	LP04
HE2A HE2D HE2E HE2H HE2I HE2M HE2N HE2O	12 Week Old Early Stage Human	Uni-ZAP XR	LP04
HE2B HE2C HE2F HE2G HE2P HE2Q	12 Week Old Early Stage Human, II	Uni-ZAP XR	LP04
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP04
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP04
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP04
HWTB HWTB HWTB	wilm's tumor	Uni-ZAP XR	LP04
HBSD	Bone Cancer, re-excision	Uni-ZAP XR	LP04
HSGB	Salivary gland, re-excision	Uni-ZAP XR	LP04
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP04
HSXA HSXB HSXC HSXD	Human Substantia Nigra	Uni-ZAP XR	LP04
HSHA HSHB HSHC	Smooth muscle, IL1b induced	Uni-ZAP XR	LP04
HOUA HOUB HOUC HOUD HOUE	Adipocytes	Uni-ZAP XR	LP04
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP04
HELA HELB HELC HELD HELE HELF HELG HELH	Endothelial cells-control	Uni-ZAP XR	LP04
HEMA HEMB HEMC HEMD HEME HEMF HEMG HEMH	Endothelial-induced	Uni-ZAP XR	LP04
HBIA HBIB HBIC	Human Brain, Striatum	Uni-ZAP XR	LP04
HHSA HHSB HHSC HHSD HHSE	Human Hypothalamus, Schizophrenia	Uni-ZAP XR	LP04
HNGA HNGB HNGC HNGD HNGE HNGF HNGG HNGH HNGI HNGJ	neutrophils control	Uni-ZAP XR	LP04
HNHA HNHB HNHC HNHD HNHE HNHF HNHG HNHH HNHI HNHI	Neutrophils IL-1 and LPS induced	Uni-ZAP XR	LP04
HSDB HSDC	STRIATUM DEPRESSION	Uni-ZAP XR	LP04

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HHPT	Hypothalamus	Uni-ZAP XR	LP04
HSAT HSAU HSAV HSAW HSAX HSAY HSAZ	Anergic T-cell	Uni-ZAP XR	LP04
HBMS HBMT HBMU HBMV HBMW HBMX	Bone marrow	Uni-ZAP XR	LP04
HOEA HOEB HOEC HOED HOEE HOEF HOEJ	Osteoblasts	Uni-ZAP XR	LP04
HAIA HAIB HAIC HAID HAIE HAIF	Epithelial-TNF $\alpha$ and INF induced	Uni-ZAP XR	LP04
HTGA HTGB HTGC HTGD	Apoptotic T-cell	Uni-ZAP XR	LP04
HMCA HMCB HMCC HMCD HMCE	Macrophage-oxLDL	Uni-ZAP XR	LP04
HMAA HMAB HMAC HMAE HMAF HMAG	Macrophage (GM-CSF treated)	Uni-ZAP XR	LP04
HPHA	Normal Prostate	Uni-ZAP XR	LP04
HPIA HPIB HPIC	LNCAP prostate cell line	Uni-ZAP XR	LP04
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP04
HOSE HOSF HOSG	Human Osteoclastoma, re-excision	Uni-ZAP XR	LP04
HTGE HTGF	Apoptotic T-cell, re-excision	Uni-ZAP XR	LP04
HMAJ HMAK	H Macrophage (GM-CSF treated), re-excision	Uni-ZAP XR	LP04
HACB HACC HACD	Human Adipose Tissue, re-excision	Uni-ZAP XR	LP04
HFPA	H. Frontal Cortex, Epileptic	Uni-ZAP XR	LP04
HFAA HFAB HFAC HFAD HFAE	Alzheimers, spongy change	Uni-ZAP XR	LP04
HFAM	Frontal Lobe, Dementia	Uni-ZAP XR	LP04
HMIA HMIB HMIC	Human Manic Depression Tissue	Uni-ZAP XR	LP04
HTSA HTSE HTSF HTSG HTSH	Human Thymus	pBS	LP05
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBS	LP05
HSAA HSAB HSAC	HSA 172 Cells	pBS	LP05
HSBA HSBB HSBC HSBM	HSC172 cells	pBS	LP05
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBS	LP05
HJBA HJBB HJBC HJBD	Jurkat T-Cell, S phase	pBS	LP05
HAFA HAFB	Aorta endothelial cells + TNF- $\alpha$	pBS	LP05
HAWA HAWB HAWC	Human White Adipose	pBS	LP05
HTNA HTNB	Human Thyroid	pBS	LP05
HONA	Normal Ovary, Premenopausal	pBS	LP05
HARA HARB	Human Adult Retina	pBS	LP05
HLJA HLJB	Human Lung	pCMVSPORT 1	LP06
HOFM HOFN HOFO	H. Ovarian Tumor, II, OV5232	pCMVSPORT 2.0	LP07
HOGA HOGB HOGC	OV 10-3-95	pCMVSPORT 2.0	LP07
HCGL	CD34+cells, II	pCMVSPORT 2.0	LP07
HDLA	Hodgkin's Lymphoma I	pCMVSPORT 2.0	LP07
HDTA HDTB HDTC HDTD HDTE	Hodgkin's Lymphoma II	pCMVSPORT 2.0	LP07
HKAA HKAB HKAC HKAD HKAE HKAF HKAG HKAH	Keratinocyte	pCMVSPORT2.0	LP07
HCIM	CAPFINDER, Crohn's Disease, lib 2	pCMVSPORT 2.0	LP07
HKAL	Keratinocyte, lib 2	pCMVSPORT2.0	LP07
HKAT	Keratinocyte, lib 3	pCMVSPORT2.0	LP07
HNDA	Nasal polyps	pCMVSPORT2.0	LP07
HDRA	H. Primary Dendritic Cells, lib 3	pCMVSPORT2.0	LP07



Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HOHA HOHB HOHC	Human Osteoblasts II	pCMVSPORT2.0	LP07
HLDA HLDB HLDC	Liver, Hepatoma	pCMVSPORT3.0	LP08
HLDN HLDO HLDP	Human Liver, normal	pCMVSPORT3.0	LP08
HMTA	pBMC stimulated w/ poly I/C	pCMVSPORT3.0	LP08
HNTA	NTERA2, control	pCMVSPORT3.0	LP08
HDP A HDPB HDP C HDPD HDPF HDPG HDPH HDPI HDPJ HDPK	Primary Dendritic Cells, lib 1	pCMVSPORT3.0	LP08
HDP M HDP N HDPO HDP P	Primary Dendritic cells, frac 2	pCMVSPORT3.0	LP08
HMUA HMUB HMUC	Myeloid Progenitor Cell Line	pCMVSPORT3.0	LP08
HHEA HHEB HHEC HHED	T Cell helper I	pCMVSPORT3.0	LP08
HHEM HHEN HHEO HHEP	T cell helper II	pCMVSPORT3.0	LP08
HEQA HEQB HEQC	Human endometrial stromal cells	pCMVSPORT3.0	LP08
HJMA HJMB	Human endometrial stromal cells-treated with progesterone	pCMVSPORT3.0	LP08
HSWA HSWB HSWC	Human endometrial stromal cells-treated with estradiol	pCMVSPORT3.0	LP08
HSYA HSYB HSYC	Human Thymus Stromal Cells	pCMVSPORT3.0	LP08
HLWA HLWB HLWC	Human Placenta	pCMVSPORT3.0	LP08
HRAA HRAB HRAC	Rejected Kidney, lib 4	pCMVSPORT3.0	LP08
HMTM	PCR, pBMC I/C treated	PCR II	LP09
HMJA	H. Meningioma, M6	pSport 1	LP10
HMKA HMKB HMKC HMKD HMKE	H. Meningioma, M1	pSport 1	LP10
HUSG HUSI	Human umbilical vein endothelial cells, IL-4 induced	pSport 1	LP10
HUSX HUSY	Human Umbilical Vein Endothelial Cells, uninduced	pSport 1	LP10
HOFA	Ovarian Tumor 1, OV5232	pSport 1	LP10
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport 1	LP10
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport 1	LP10
HADA HADC HADD HADE HADF HADG	Human Adipose	pSport 1	LP10
HOVA HOVB HOVC	Human Ovary	pSport 1	LP10
HTWB HTWC HTWD HTWE HTWF	Resting T-Cell Library, II	pSport 1	LP10
HMMA	Spleen metastatic melanoma	pSport 1	LP10
HLYA HLYB HLYC HLYD HLYE	Spleen, Chronic lymphocytic leukemia	pSport 1	LP10
HCGA	CD34+ cell, I	pSport 1	LP10
HEOM HEON	Human Eosinophils	pSport 1	LP10
HTDA	Human Tonsil, Lib 3	pSport 1	LP10
HSPA	Salivary Gland, Lib 2	pSport 1	LP10
HCHA HCHB HCHC	Breast Cancer cell line, MDA 36	pSport 1	LP10
HCHM HCHN	Breast Cancer Cell line, angiogenic	pSport 1	LP10
HCIA	Crohn's Disease	pSport 1	LP10
HDAA HDAB HDAC	HEL cell line	pSport 1	LP10
HABA	Human Astrocyte	pSport 1	LP10
HUFA HUFB HUFC	Ulcerative Colitis	pSport 1	LP10
HNTM	NTERA2 + retinoic acid, 14 days	pSport 1	LP10
HDQA	Primary Dendritic cells, CapFinder2, frac 1	pSport 1	LP10
HDQM	Primary Dendritic Cells, CapFinder, frac	pSport 1	LP10

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	2		
HLDX	Human Liver, normal.CapFinder	pSport 1	LP10
HULA HULB HULC	Human Dermal Endothelial Cells.untreated	pSport1	LP10
HUMA	Human Dermal Endothelial cells.treated	pSport1	LP10
HCJA	Human Stromal Endometrial fibroblasts, untreated	pSport1	LP10
HCJM	Human Stromal endometrial fibroblasts, treated w/ estradiol	pSport1	LP10
HEDA	Human Stromal endometrial fibroblasts, treated with progesterone	pSport1	LP10
HFNA	Human ovary tumor cell OV350721	pSport1	LP10
HKGA HKGB HKGC HKGD	Merkel Cells	pSport1	LP10
HISA HISB HISC	Pancreas Islet Cell Tumor	pSport1	LP10
HLSA	Skin, burned	pSport1	LP10
HBZA	Prostate.BPH, Lib 2	pSport 1	LP10
HBZS	Prostate BPH,Lib 2, subtracted	pSport 1	LP10
HFIA HFIB HFIC	Synovial Fibroblasts (control)	pSport 1	LP10
HFIH HFII HFIJ	Synovial hypoxia	pSport 1	LP10
HFIT HFIU HFIV	Synovial IL-1/TNF stimulated	pSport 1	LP10
HGCA	Mesangial cell, frac 1	pSport1	LP10
HMVA HMVB HMVC	Bone Marrow Stromal Cell, untreated	pSport1	LP10
HFIX HFYI HFIZ	Synovial Fibroblasts (IL1/TNF), sub1	pSport1	LP10
HFOX HFOY HFOZ	Synovial hypoxia-RSF subtracted	pSport1	LP10
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP11
HLIA HLIB HLIC	Human Liver	pCMVSPORT 1	LP012
HHBA HHBB HHBC HHBD HHBE	Human Heart	pCMVSPORT 1	LP012
HBBA HBBB	Human Brain	pCMVSPORT 1	LP012
HLJA HLJB HLJC HLJD HLJE	Human Lung	pCMVSPORT 1	LP012
HOGA HOGB HOGC	Ovarian Tumor	pCMVSPORT 2.0	LP012
HTJM	Human Tonsils, Lib 2	pCMVSPORT 2.0	LP012
HAMF HAMG	KMH2	pCMVSPORT 3.0	LP012
HABA HAJB HAJC	L428	pCMVSPORT 3.0	LP012
HWBA HWBB HWBC HWBD HWBE	Dendritic cells, pooled	pCMVSPORT 3.0	LP012
HWAA HWAB HWAC HWAD HWAE	Human Bone Marrow, treated	pCMVSPORT 3.0	LP012
HYAA HYAB HYAC	B Cell lymphoma	pCMVSPORT 3.0	LP012
HWHG HWHH HWHI	Healing groin wound, 6.5 hours post incision	pCMVSPORT 3.0	LP012
HWHP HWHQ HWHR	Healing groin wound; 7.5 hours post incision	pCMVSPORT 3.0	LP012
HARM	Healing groin wound - zero hr post-incision (control)	pCMVSPORT 3.0	LP012
HBIM	Olfactory epithelium; nasalcavity	pCMVSPORT 3.0	LP012
HWDA	Healing Abdomen wound; 70&90 min post incision	pCMVSPORT 3.0	LP012
HWEA	Healing Abdomen Wound;15 days post incision	pCMVSPORT 3.0	LP012
HWJA	Healing Abdomen Wound;21&29 days	pCMVSPORT 3.0	LP012
HNAL	Human Tongue, frac 2	pSport1	LP012
HMJA	H. Meningioma, M6	pSport1	LP012
HMKA HMKB HMKC HMKD HMKE	H. Meningioma, M1	pSport1	LP012

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HOFA	Ovarian Tumor I, OV5232	pSport1	LP012
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport1	LP012
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport1	LP012
HMMA HMMB HMMC	Spleen metastatic melanoma	pSport1	LP012
HTDA	Human Tonsil, Lib 3	pSport1	LP012
HDBA	Human Fetal Thymus	pSport1	LP012
HDDA	Pericardium	pSport1	LP012
HBZA	Prostate, BPH, Lib 2	pSport1	LP012
HWCA	Larynx tumor	pSport1	LP012
HWKA	Normal lung	pSport1	LP012
HSMB	Bone marrow stroma, treated	pSport1	LP012
HBHM	Normal trachea	pSport1	LP012
HLFC	Human Larynx	pSport1	LP012
HLRB	Siebben Polyposis	pSport1	LP012
HNIA	Mammary Gland	pSport1	LP012
HNJB	Palate carcinoma	pSport1	LP012
HNKA	Palate normal	pSport1	LP012
HMZA	Pharynx carcinoma	pSport1	LP012
HABG	Cheek Carcinoma	pSport1	LP012
HMZM	Pharynx Carcinoma	pSport1	LP012
HDRM	Larynx Carcinoma	pSport1	LP012
HVAA	Pancreas normal PCA4 No	pSport1	LP012
HICA	Tongue carcinoma	pSport1	LP012
HUKA HUKB HUKC HUKD HUKF	Human Uterine Cancer	Lambda ZAP II	LP013
HFFA	Human Fetal Brain, random primed	Lambda ZAP II	LP013
HTUA	Activated T-cell labeled with 4-thioluri	Lambda ZAP II	LP013
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP013
HMEB	Human microvascular Endothelial cells, fract. B	Lambda ZAP II	LP013
HUSH	Human Umbilical Vein Endothelial cells, fract. A, re-excision	Lambda ZAP II	LP013
HLQC HLQD	Hepatocellular tumor, re-excision	Lambda ZAP II	LP013
HTWJ HTWK HTWL	Resting T-cell, re-excision	Lambda ZAP II	LP013
HF6S	Human Whole 6 week Old Embryo (II), subt	pBluescript	LP013
HHPS	Human Hippocampus, subtracted	pBluescript	LP013
HLIS	LNCAP, differential expression	pBluescript	LP013
HLHS HLHT	Early Stage Human Lung, Subtracted	pBluescript	LP013
HSUS	Supt cells, cyclohexamide treated, subtracted	pBluescript	LP013
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBluescript	LP013
HSDS	H. Striatum Depression, subtracted	pBluescript	LP013
HPTZ	Human Pituitary, Subtracted VII	pBluescript	LP013
HSDX	H. Striatum Depression, subt II	pBluescript	LP013
HSDZ	H. Striatum Depression, subt	pBluescript	LP013
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBluescript SK-	LP013
HRTA	Colorectal Tumor	pBluescript SK-	LP013
HSBA HSBB HSBC HSBM	HSC172 cells	pBluescript SK-	LP013
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBluescript SK-	LP013
HJBA HJBB HJBC HJBD	Jurkat T-cell, S1 phase	pBluescript SK-	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HTNA HTNB	Human Thyroid	pBluescript SK-	LP013
HAHA HAHB	Human Adult Heart	Uni-ZAP XR	LP013
HE6A	Whole 6 week Old Embryo	Uni-ZAP XR	LP013
HFC A HFCB HFCC HFCD HFCE	Human Fetal Brain	Uni-ZAP XR	LP013
HFKC HFKD HFKE HFKF HFKG	Human Fetal Kidney	Uni-ZAP XR	LP013
HGBA HGBD HGBE HGBF HGBG	Human Gall Bladder	Uni-ZAP XR	LP013
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP013
HTEA HTEB HTEC HTEF HTEE	Human Testes	Uni-ZAP XR	LP013
HTTA HTTB HTTC HTTD HTTE	Human Testes Tumor	Uni-ZAP XR	LP013
HYBA HYBB	Human Fetal Bone	Uni-ZAP XR	LP013
HFLA	Human Fetal Liver	Uni-ZAP XR	LP013
HHFB HHFC HHFD HHFE HHFF	Human Fetal Heart	Uni-ZAP XR	LP013
HUVB HUV C HUVD HUVE	Human Umbilical Vein, End. remake	Uni-ZAP XR	LP013
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP013
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP013
HTAA HTAB HTAC HTAD HTAE	Human Activated T-cells	Uni-ZAP XR	LP013
HFEA HFEB HFEC	Human Fetal Epithelium (skin)	Uni-ZAP XR	LP013
HJPA HJPB HJPC HJPD	Human Jurkat Membrane Bound Polysomes	Uni-ZAP XR	LP013
HESA	Human Epithelioid Sarcoma	Uni-ZAP XR	LP013
HALS	Human Adult Liver, Subtracted	Uni-ZAP XR	LP013
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP013
HCAA HCAB HCAC	Cem cells, cyclohexamide treated	Uni-ZAP XR	LP013
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP013
HE9A HE9B HE9C HE9D HE9E	Nine Week Old Early Stage Human	Uni-ZAP XR	LP013
HSFA	Human Fibrosarcoma	Uni-ZAP XR	LP013
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP013
HTRA	Human Trachea Tumor	Uni-ZAP XR	LP013
HE2A HE2D HE2E HE2H HE2I	12 Week Old Early Stage Human	Uni-ZAP XR	LP013
HE2B HE2C HE2F HE2G HE2P	12 Week Old Early Stage Human, II	Uni-ZAP XR	LP013
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP013
HBGA	Human Primary Breast Cancer	Uni-ZAP XR	LP013
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP013
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP013
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP013
HTOA HTOD HTOE HTOF HTOG	human tonsils	Uni-ZAP XR	LP013
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP013
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP013
HOQB	Human OB HOS treated (1 nM E2) fraction I	Uni-ZAP XR	LP013
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP013
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP013
HROA HROC	HUMAN STOMACH	Uni-ZAP XR	LP013
HBJA HBJB HBJC HBJD HBJE	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP013
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP013
HCPA	Corpus Callosum	Uni-ZAP XR	LP013
HSOA	stomach cancer (human)	Uni-ZAP XR	LP013
HERA	SKIN	Uni-ZAP XR	LP013
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP013
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HWTB HWTB HWTB	wilm's tumor	Uni-ZAP XR	LP013
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP013
HAPN HAPN HAPN HAPQ HAPR	Human Adult Pulmonary;re-excision	Uni-ZAP XR	LP013
HLTG HLTH	Human T-cell lymphoma;re-excision	Uni-ZAP XR	LP013
HAHC HAHD HAHE	Human Adult Heart;re-excision	Uni-ZAP XR	LP013
HAGA HAGB HAGC HAGD HAGE	Human Amygdala	Uni-ZAP XR	LP013
HSJA HSJB HSJC	Smooth muscle-IL1b induced	Uni-ZAP XR	LP013
HSJA HSJB HSJC	Smooth muscle, IL1b induced	Uni-ZAP XR	LP013
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP013
HPJA HPJB HPJC	LNCAP prostate cell line	Uni-ZAP XR	LP013
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP013
HBTA	Bone Marrow Stroma, TNF&LPS ind	Uni-ZAP XR	LP013
HMCF HMCG HMCH HMCI HMCJ	Macrophage-oxLDL; re-excision	Uni-ZAP XR	LP013
HAGG HAGH HAGI	Human Amygdala;re-excision	Uni-ZAP XR	LP013
HACA	H. Adipose Tissue	Uni-ZAP XR	LP013
HKFB	K562 + PMA (36 hrs);re-excision	ZAP Express	LP013
HCWT HCWU HCWV	CD34 positive cells (cord blood);re-ex	ZAP Express	LP013
HBWA	Whole brain	ZAP Express	LP013
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP013
HAVM	Temporal cortex-Alzheimer	pT-Adv	LP014
HAVT	Hippocampus, Alzheimer Subtracted	pT-Adv	LP014
HHAS	CHME Cell Line	Uni-ZAP XR	LP014
HBJR	Larynx normal	pSport 1	LP014
HWLE HWLF HWLG HWLH	Colon Normal	pSport 1	LP014
HCRM HCRN HCRO	Colon Carcinoma	pSport 1	LP014
HWLI HWLJ HWLK	Colon Normal	pSport 1	LP014
HWLQ HWLR HWLS HWLT	Colon Tumor	pSport 1	LP014
HBFM	Gastrocnemius Muscle	pSport 1	LP014
HBOD HBOE	Quadriceps Muscle	pSport 1	LP014
HBKD HBKE	Soleus Muscle	pSport 1	LP014
HCCM	Pancreatic Langerhans	pSport 1	LP014
HWGA	Larynx carcinoma	pSport 1	LP014
HWGM HWGN	Larynx carcinoma	pSport 1	LP014
HWLA HWLB HWLC	Normal colon	pSport 1	LP014
HWLM HWLN	Colon Tumor	pSport 1	LP014
HVAM HVAN HVAO	Pancreas Tumor	pSport 1	LP014
HWGQ	Larynx carcinoma	pSport 1	LP014
HAQM HAQN	Salivary Gland	pSport 1	LP014
HASM	Stomach; normal	pSport 1	LP014
HBCM	Uterus; normal	pSport 1	LP014
HCDM	Testis; normal	pSport 1	LP014
HDJM	Brain; normal	pSport 1	LP014
HEFM	Adrenal Gland;normal	pSport 1	LP014
HBAA	Rectum normal	pSport 1	LP014
HFDM	Rectum tumour	pSport 1	LP014
HGAM	Colon, normal	pSport 1	LP014
HHMM	Colon, tumour	pSport 1	LP014
HCLB HCLC	Human Lung Cancer	Lambda Zap II	LP015
HRLA	L1 Cell line	ZAP Express	LP015

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HHAM	Hypothalamus. Alzheimer's	pCMVSPORT 3.0	LP015
HKBA	Ku 812F Basophils Line	pSport 1	LP015
HS2S	Saos2. Dexamethosone Treated	pSport 1	LP016
HA5A	Lung Carcinoma A549 TNFalpha activated	pSport 1	LP016
HTFM	TF-1 Cell Line GM-CSF Treated	pSport 1	LP016
HYAS	Thyroid Tumour	pSport 1	LP016
HUTS	Larynx Normal	pSport 1	LP016
HXOA	Larynx Tumor	pSport 1	LP016
HEAH	Ea.hy.926 cell line	pSport 1	LP016
HINA	Adenocarcinoma Human	pSport 1	LP016
HRMA	Lung Mesothelium	pSport 1	LP016
HLCL	Human Pre-Differentiated Adipocytes	Uni-Zap XR	LP017
HS2A	Saos2 Cells	pSport 1	LP020
HS2I	Saos2 Cells; Vitamin D3 Treated	pSport 1	LP020
HUCM	CHME Cell Line, untreated	pSport 1	LP020
HEPN	Aryepiglottis Normal	pSport 1	LP020
HPSN	Sinus Piniiformis Tumour	pSport 1	LP020
HNSA	Stomach Normal	pSport 1	LP020
HNSM	Stomach Tumour	pSport 1	LP020
HNLA	Liver Normal Met5No	pSport 1	LP020
HUTA	Liver Tumour Met 5 Tu	pSport 1	LP020
HOCN	Colon Normal	pSport 1	LP020
HOCT	Colon Tumor	pSport 1	LP020
HTNT	Tongue Tumour	pSport 1	LP020
HLXN	Larynx Normal	pSport 1	LP020
HLXT	Larynx Tumour	pSport 1	LP020
HTYN	Thymus	pSport 1	LP020
HPLN	Placenta	pSport 1	LP020
HTNG	Tongue Normal	pSport 1	LP020
HZAA	Thyroid Normal (SDCA2 No)	pSport 1	LP020
HWES	Thyroid Thyroiditis	pSport 1	LP020
HFHD	Ficolled Human Stromal Cells, 5Fu treated	pTriplEx2	LP021
HFHM,HFHN	Ficolled Human Stromal Cells, Untreated	pTriplEx2	LP021
HPCI	Hep G2 Cells, lambda library	lambda Zap-CMV XR	LP021
HBCA,HBCB,HBCC	H. Lymph node breast Cancer	Uni-ZAP XR	LP021
HCOK	Chondrocytes	pSPORT1	LP022
HDCA, HDCB, HDCC	Dendritic Cells From CD34 Cells	pSPORT1	LP022
HDMA, HDMB	CD40 activated monocyte dendritic cells	pSPORT1	LP022
HDDM, HDDN, HDDO	LPS activated derived dendritic cells	pSPORT1	LP022
HPCR	Hep G2 Cells, PCR library	lambda Zap-CMV XR	LP022
HAAA, HAAB, HAAC	Lung, Cancer (4005313A3): Invasive Poorly Differentiated Lung Adenocarcinoma	pSPORT1	LP022
HIPA, HIPB, HIPC	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	pSPORT1	LP022
HOOH, HOOI	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low	pSPORT1	LP022

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	Malignant Pot		
HIDA	Lung, Normal: (4005313 B1)	pSPORT1	LP022
HUJA.HUJB.HUJC.HUJD.HUJE	B-Cells	pCMVSPORT 3.0	LP022
HNOA.HNOB.HNOC.HNOD	Ovary, Normal: (9805C040R)	pSPORT1	LP022
HNLM	Lung, Normal: (4005313 B1)	pSPORT1	LP022
HSCL	Stromal Cells	pSPORT1	LP022
HAAX	Lung, Cancer: (4005313 A3) Invasive Poorly-differentiated Metastatic lung adenocarcinoma	pSPORT1	LP022
HUUA.HUUB.HUUC.HUUD	B-cells (unstimulated)	pTriplEx2	LP022
HWWA.HWWB.HWWC.HWWD,HWE.HWWF.HWWG	B-cells (stimulated)	pSPORT1	LP022
HCCC	Colon, Cancer: (9808C064R)	pCMVSPORT 3.0	LP023
HPDO HPDP HPDQ HPDR HPD	Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma	pSport 1	LP023
HPCO HPCP HPCQ HPCT	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	pSport 1	LP023
HOCM HOCO HOCB HOCQ	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	pSport 1	LP023
HCBM HCBN HCBO	Breast, Cancer: (4004943 A5)	pSport 1	LP023
HNBT HNBH HNBV	Breast, Normal: (4005522B2)	pSport 1	LP023
HBCP HBCQ	Breast, Cancer: (4005522 A2)	pSport 1	LP023
HBCJ	Breast, Cancer: (9806C012R)	pSport 1	LP023
HSAM HSAN	Stromal cells 3.88	pSport 1	LP023
HVCA HVCB HVCC HVCD	Ovary, Cancer: (4004332 A2)	pSport 1	LP023
HSCK HSEN HSEO	Stromal cells (HBM3.18)	pSport 1	LP023
HSCP HSCQ	stromal cell clone 2.5	pSport 1	LP023
HUXA	Breast Cancer: (4005385 A2)	pSport 1	LP023
HCOM HCON HCOO HCOP HCOQ	Ovary, Cancer (4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	pSport 1	LP023
HBNM	Breast, Cancer: (9802C020E)	pSport 1	LP023
HVVA HVVB HVVC HVVD HVVE	Human Bone Marrow, treated	pSport 1	LP023

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 5. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to the nucleotide sequence of SEQ ID NO:X.

5        Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with  $^{32}\text{P}$ - $\gamma$ -ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, Cold Spring, NY (1982).) The plasmid  
10        mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using  
15        Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

          Alternatively, two primers of 17-20 nucleotides derived from both ends of the  
20        nucleotide sequence of SEQ ID NO:X are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25  $\mu\text{l}$  of reaction mixture with 0.5  $\mu\text{g}$  of the above cDNA template. A convenient reaction mixture is 1.5-5 mM  $\text{MgCl}_2$ , 0.01% (w/v) gelatin, 20  $\mu\text{M}$  each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of  
25        Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR  
30        product is verified to be the selected sequence by subcloning and sequencing the DNA product.

          Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not



limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., Nucleic Acids Res. 21(7):1683-1684 (1993).)

5 Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full  
10 length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the  
15 RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis  
20 using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

25

***Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide***

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the sequence corresponding to SEQ ID NO:X, according to the method  
30 described in Example 1. (See also, Sambrook.)

***Example 3: Tissue specific expression analysis***

The Human Genome Sciences, Inc. (HGS) database is derived from sequencing tissue specific cDNA libraries. Libraries generated from a particular tissue are selected and the specific tissue expression pattern of EST groups or assembled contigs within these libraries is determined by comparison of the expression patterns of those groups or contigs within the entire database. ESTs which show tissue specific expression are selected.

The original clone from which the specific EST sequence was generated, is obtained from the catalogued library of clones and the insert amplified by PCR using methods known in the art. The PCR product is denatured then transferred in 96 well format to a nylon membrane (Schleicher and Schuell) generating an array filter of tissue specific clones. Housekeeping genes, maize genes, and known tissue specific genes are included on the filters. These targets can be used in signal normalization and to validate assay sensitivity. Additional targets are included to monitor probe length and specificity of hybridization.

Radioactively labeled hybridization probes are generated by first strand cDNA synthesis per the manufacturer's instructions (Life Technologies) from mRNA/RNA samples prepared from the specific tissue being analyzed. The hybridization probes are purified by gel exclusion chromatography, quantitated, and hybridized with the array filters in hybridization bottles at 65°C overnight. The filters are washed under stringent conditions and signals are captured using a Fuji phosphorimager.

Data is extracted using AIS software and following background subtraction, signal normalization is performed. This includes a normalization of filter-wide expression levels between different experimental runs. Genes that are differentially expressed in the tissue of interest are identified and the full length sequence of these clones is generated.

***Example 4: Chromosomal Mapping of the Polynucleotides***

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute

cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR  
5 fragment in the particular somatic cell hybrid.

***Example 5: Bacterial Expression of a Polypeptide***

A polynucleotide encoding a polypeptide of the present invention is amplified using  
10 PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial  
15 expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp<sup>r</sup>), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is  
20 ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan<sup>r</sup>). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is  
25 isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.<sup>600</sup>) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto  
30 pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid (5 "Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 (10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The (15 recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM imidazole. Imidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. (20 The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase (25 gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, (30 BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction

sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express  
5 protein in a bacterial system.

***Example 6: Purification of a Polypeptide from an Inclusion Body***

The following alternative method can be used to purify a polypeptide expressed in *E*  
10 *coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell  
15 paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfluidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then  
20 mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is  
25 discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous  
30 stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16  $\mu$ m membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column  
5 is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of  
10 water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging  
15 from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant  $A_{280}$  monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from  
20 Commassie blue stained 16% SDS-PAGE gel when 5  $\mu$ g of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

#### *Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System*

25

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of  
30 recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under

control of a weak *Drosophila* promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

5 Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., *Virology* 170:31-39 (1989).

10 Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon, is amplified using the PCR protocol described in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard  
15 methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with  
20 appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("GeneClean" BIO 101 Inc., La Jolla, Ca.).

25 The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the  
30 cloned fragment is confirmed by DNA sequencing.

Five  $\mu$ g of a plasmid containing the polynucleotide is co-transfected with 1.0  $\mu$ g of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA",

Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One  $\mu\text{g}$  of BaculoGold™ virus DNA and 5  $\mu\text{g}$  of the plasmid are mixed in a sterile well of a microtiter plate containing 50  $\mu\text{l}$  of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10  $\mu\text{l}$  Lipofectin plus 90  $\mu\text{l}$  Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200  $\mu\text{l}$  of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5  $\mu\text{Ci}$  of  $^{35}\text{S}$ -methionine and 5  $\mu\text{Ci}$   $^{35}\text{S}$ -cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.



*Example 8: Expression of a Polypeptide in Mammalian Cells*

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLV, HIV and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSPORT 2.0, and pCMVSPORT 3.0. Mammalian host cells that could be used include, human HeLa, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as DHFR, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used

for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No. 209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the vector does not need a second signal peptide. Alternatively, if a naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five  $\mu$ g of the expression plasmid pC6 or pC4 is cotransfected with 0.5  $\mu$ g of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10,

25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well  
5 plates containing even higher concentrations of methotrexate (1  $\mu$ M, 2  $\mu$ M, 5  $\mu$ M, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200  $\mu$ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

#### 10 *Example 9: Protein Fusions*

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding  
15 protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the half-life time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion  
20 proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

25 Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be  
30 ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the

vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the polypeptide of the present invention, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

10 GGGATCCGGAGCCCAAATCTTCTGACAAAACCTCACACATGCCCACCGTGCCCAG  
CACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCAAACCCAAGGA  
CACCTCATGATCTCCCGACTCCTGAGGTCACATGCGTGGTGGTGGACGTAAGC  
CACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAT  
AATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC  
15 AGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGC  
AAGGTCTCCAACAAAGCCCTCCCAACCCCCATCGAGAAAACCATCTCCAAGCC  
AAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAG  
CTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAAGC  
GACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGAC  
20 CACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACC  
GTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCAT  
GAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAAT  
GAGTGCGACGGCCGCGACTCTAGAGGAT (SEQ ID NO:837)

25 *Example 10: Production of an Antibody from a Polypeptide*

#### a) Hybridoma Technology

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) As one example of such methods, cells expressing polypeptide of the present invention are administered to an animal to induce the production of sera containing polyclonal antibodies. In a preferred method, a preparation of polypeptide

of the present invention is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

Monoclonal antibodies specific for polypeptide of the present invention are prepared using hybridoma technology. (Kohler et al., *Nature* 256:495 (1975); Kohler et al., *Eur. J. Immunol.* 6:511 (1976); Kohler et al., *Eur. J. Immunol.* 6:292 (1976); Hammerling et al., in: *Monoclonal Antibodies and T-Cell Hybridomas*, Elsevier, N.Y., pp. 563-681 (1981)). In general, an animal (preferably a mouse) is immunized with polypeptide of the present invention or, more preferably, with a secreted polypeptide of the present invention-expressing cell. Such polypeptide-expressing cells are cultured in any suitable tissue culture medium, preferably in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (*Gastroenterology* 80:225-232 (1981)). The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide of the present invention.

Alternatively, additional antibodies capable of binding to polypeptide of the present invention can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the polypeptide of the present invention-specific antibody can be blocked by polypeptide of the present invention. Such antibodies comprise anti-idiotypic antibodies to the polypeptide of the present invention-specific antibody and are used to immunize an animal to induce formation of further polypeptide of the present invention-specific antibodies.

For in vivo use of antibodies in humans, an antibody is "humanized". Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric and humanized antibodies are known in the art and are discussed herein. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

**b) Isolation Of Antibody Fragments Directed Against Polypeptide of the Present Invention From A Library Of scFvs**

Naturally occurring V-genes isolated from human PBLs are constructed into a library of antibody fragments which contain reactivities against polypeptide of the present invention to which the donor may or may not have been exposed (see e.g., U.S. Patent 5,885,793 incorporated herein by reference in its entirety).

*Rescue of the Library.* A library of scFvs is constructed from the RNA of human PBLs as described in PCT publication WO 92/01047. To rescue phage displaying antibody fragments, approximately 10<sup>9</sup> E. coli harboring the phagemid are used to inoculate 50 ml of 2xTY containing 1% glucose and 100 µg/ml of ampicillin (2xTY-AMP-GLU) and grown to an O.D. of 0.8 with shaking. Five ml of this culture is used to inoculate 50 ml of 2xTY-AMP-GLU, 2 x 10<sup>8</sup> TU of delta gene 3 helper (M13 delta gene III, see PCT publication WO 92/01047) are added and the culture incubated at 37°C for 45 minutes without shaking and then at 37°C for 45 minutes with shaking. The culture is centrifuged at 4000 r.p.m. for 10 min. and the pellet resuspended in 2 liters of 2xTY containing 100 µg/ml ampicillin and 50 µg/ml kanamycin and grown overnight. Phage are prepared as described in PCT publication WO 92/01047.

M13 delta gene III is prepared as follows: M13 delta gene III helper phage does not encode gene III protein, hence the phage(mid) displaying antibody fragments have a greater avidity of binding to antigen. Infectious M13 delta gene III particles are made by growing the helper phage in cells harboring a pUC19 derivative supplying the wild type gene III protein during phage morphogenesis. The culture is incubated for 1 hour at 37° C without shaking and then for a further hour at 37°C with shaking. Cells are spun down (IEC-Centra

8,400 r.p.m. for 10 min), resuspended in 300 ml 2xTY broth containing 100 µg ampicillin/ml and 25 µg kanamycin/ml (2xTY-AMP-KAN) and grown overnight, shaking at 37°C. Phage particles are purified and concentrated from the culture medium by two PEG-precipitations (Sambrook et al., 1990), resuspended in 2 ml PBS and passed through a 0.45 µm filter (Minisart NML; Sartorius) to give a final concentration of approximately 10<sup>13</sup> transducing units/ml (ampicillin-resistant clones).

*Panning of the Library.* Immunotubes (Nunc) are coated overnight in PBS with 4 ml of either 100 µg/ml or 10 µg/ml of a polypeptide of the present invention. Tubes are blocked with 2% Marvel-PBS for 2 hours at 37°C and then washed 3 times in PBS. Approximately 10<sup>13</sup> TU of phage is applied to the tube and incubated for 30 minutes at room temperature tumbling on an over and under turntable and then left to stand for another 1.5 hours. Tubes are washed 10 times with PBS 0.1% Tween-20 and 10 times with PBS. Phage are eluted by adding 1 ml of 100 mM triethylamine and rotating 15 minutes on an under and over turntable after which the solution is immediately neutralized with 0.5 ml of 1.0M Tris-HCl, pH 7.4. Phage are then used to infect 10 ml of mid-log E. coli TG1 by incubating eluted phage with bacteria for 30 minutes at 37°C. The E. coli are then plated on TYE plates containing 1% glucose and 100 µg/ml ampicillin. The resulting bacterial library is then rescued with delta gene 3 helper phage as described above to prepare phage for a subsequent round of selection. This process is then repeated for a total of 4 rounds of affinity purification with tube-washing increased to 20 times with PBS, 0.1% Tween-20 and 20 times with PBS for rounds 3 and 4.

*Characterization of Binders.* Eluted phage from the 3rd and 4th rounds of selection are used to infect E. coli HB 2151 and soluble scFv is produced (Marks, et al., 1991) from single colonies for assay. ELISAs are performed with microtitre plates coated with either 10 pg/ml of the polypeptide of the present invention in 50 mM bicarbonate pH 9.6. Clones positive in ELISA are further characterized by PCR fingerprinting (see, e.g., PCT publication WO 92/01047) and then by sequencing. These ELISA positive clones may also be further characterized by techniques known in the art, such as, for example, epitope mapping, binding affinity, receptor signal transduction, ability to block or competitively inhibit antibody/antigen binding, and competitive agonistic or antagonistic activity.

*Example 11: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide*

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X; and/or the nucleotide sequence of the related cDNA in the cDNA clone contained in a deposited library. Suggested PCR conditions consist of 35 cycles at 95 degrees C for 30 seconds; 60-120 seconds at 52-58 degrees C; and 60-120 seconds at 70 degrees C, using buffer solutions described in Sidransky et al., Science 252:706 (1991).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton et al., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-triphosphate (Boehringer Mannheim), and FISH performed as described in Johnson et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image



collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

*Example 12: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample*

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

*Example 13: Formulation*

The invention also provides methods of treatment and/or prevention of diseases or disorders (such as, for example, any one or more of the diseases or disorders disclosed  
5 herein) by administration to a subject of an effective amount of a Therapeutic. By therapeutic is meant a polynucleotides or polypeptides of the invention (including fragments and variants), agonists or antagonists thereof, and/or antibodies thereto, in combination with a pharmaceutically acceptable carrier type (e.g., a sterile carrier).

The Therapeutic will be formulated and dosed in a fashion consistent with good  
10 medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the Therapeutic alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of the  
15 Therapeutic administered parenterally per dose will be in the range of about 1 µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given  
20 continuously, the Therapeutic is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

25 Therapeutics can be are administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any. The term "parenteral" as used herein refers to modes of  
30 administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics are administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray.

5 "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release  
10 systems. Suitable examples of sustained-release Therapeutics include suitable polymeric materials (such as, for example, semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules), suitable hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, and sparingly soluble derivatives (such as, for example, a sparingly soluble salt).

15 Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman et al., *Biopolymers* 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (Langer et al., *J. Biomed. Mater. Res.* 15:167-277 (1981), and Langer, *Chem. Tech.* 12:98-105 (1982)), ethylene vinyl acetate (Langer et al., *Id.*) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988).

20 Sustained-release Therapeutics also include liposomally entrapped Therapeutics of the invention (*see* generally, Langer, *Science* 249:1527-1533 (1990); Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 317 -327 and 353-365 (1989)). Liposomes containing the Therapeutic are prepared by methods known per se: DE 3,218,121; Epstein et al., *Proc. Natl. Acad. Sci. (USA)* 82:3688-3692 (1985); Hwang et al., *Proc. Natl. Acad. Sci.(USA)*  
25 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being  
30 adjusted for the optimal Therapeutic.

In yet an additional embodiment, the Therapeutics of the invention are delivered by way of a pump (*see* Langer, *supra*; Sefton, *CRC Crit. Ref. Biomed. Eng.* 14:201 (1987);

Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)).

Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

For parenteral administration, in one embodiment, the Therapeutic is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to the Therapeutic.

Generally, the formulations are prepared by contacting the Therapeutic uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The Therapeutic is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any pharmaceutical used for therapeutic administration can be sterile. Sterility is

readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutics generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

5           Therapeutics ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous Therapeutic solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized Therapeutic  
10       using bacteriostatic Water-for-Injection.

          The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the Therapeutics of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products,  
15       which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the Therapeutics may be employed in conjunction with other therapeutic compounds.

          The Therapeutics of the invention may be administered alone or in combination with adjuvants. Adjuvants that may be administered with the Therapeutics of the invention  
20       include, but are not limited to, alum, alum plus deoxycholate (ImmunoAg), MTP-PE (Biocine Corp.), QS21 (Genentech, Inc.), BCG, and MPL. In a specific embodiment, Therapeutics of the invention are administered in combination with alum. In another specific embodiment, Therapeutics of the invention are administered in combination with QS-21. Further adjuvants that may be administered with the Therapeutics of the invention include,  
25       but are not limited to, Monophosphoryl lipid immunomodulator, AdjuVax 100a, QS-21, QS-18, CRL1005, Aluminum salts, MF-59, and Virosomal adjuvant technology. Vaccines that may be administered with the Therapeutics of the invention include, but are not limited to, vaccines directed toward protection against MMR (measles, mumps, rubella), polio, varicella, tetanus/diphtheria, hepatitis A, hepatitis B, haemophilus influenzae B, whooping  
30       cough, pneumonia, influenza, Lyme's Disease, rotavirus, cholera, yellow fever, Japanese encephalitis, poliomyelitis, rabies, typhoid fever, and pertussis. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or

concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the separate  
5 administration of one of the compounds or agents given first, followed by the second.

The Therapeutics of the invention may be administered alone or in combination with other therapeutic agents. Therapeutic agents that may be administered in combination with the Therapeutics of the invention, include but not limited to, other members of the TNF family, chemotherapeutic agents, antibiotics, steroidal and non-steroidal anti-inflammatories,  
10 conventional immunotherapeutic agents, cytokines and/or growth factors. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous  
15 lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

In one embodiment, the Therapeutics of the invention are administered in combination with members of the TNF family. TNF, TNF-related or TNF-like molecules that may be administered with the Therapeutics of the invention include, but are not limited  
20 to, soluble forms of TNF-alpha, lymphotoxin-alpha (LT-alpha, also known as TNF-beta), LT-beta (found in complex heterotrimer LT-alpha2-beta), OPGL, FasL, CD27L, CD30L, CD40L, 4-1BBL, DcR3, OX40L, TNF-gamma (International Publication No. WO 96/14328), AIM-I (International Publication No. WO 97/33899), endokine-alpha (International Publication No. WO 98/07880), TR6 (International Publication No. WO  
25 98/30694), OPG, and neutrokin-alpha (International Publication No. WO 98/18921, OX40, and nerve growth factor (NGF), and soluble forms of Fas, CD30, CD27, CD40 and 4-1BB, TR2 (International Publication No. WO 96/34095), DR3 (International Publication No. WO 97/33904), DR4 (International Publication No. WO 98/32856), TR5 (International Publication No. WO 98/30693), TR6 (International Publication No. WO 98/30694), TR7  
30 (International Publication No. WO 98/41629), TRANK, TR9 (International Publication No. WO 98/56892), TR10 (International Publication No. WO 98/54202), 312C2 (International Publication No. WO 98/06842), and TR12, and soluble forms CD154, CD70, and CD153.

In certain embodiments, Therapeutics of the invention are administered in combination with antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors. Nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, RETROVIR™ (zidovudine/AZT), VIDEX™ (didanosine/ddI), HIVID™ (zalcitabine/ddC), ZERIT™ (stavudine/d4T), EPIVIR™ (lamivudine/3TC), and COMBIVIR™ (zidovudine/lamivudine). Non-nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, VIRAMUNE™ (nevirapine), RESCRIPTOR™ (delavirdine), and SUSTIVA™ (efavirenz). Protease inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, CRIXIVAN™ (indinavir), NORVIR™ (ritonavir), INVIRASE™ (saquinavir), and VIRACEPT™ (nelfinavir). In a specific embodiment, antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors may be used in any combination with Therapeutics of the invention to treat AIDS and/or to prevent or treat HIV infection.

In other embodiments, Therapeutics of the invention may be administered in combination with anti-opportunistic infection agents. Anti-opportunistic agents that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, ATOVAQUONE™, ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, ETHAMBUTOL™, RIFABUTIN™, CLARITHROMYCIN™, AZITHROMYCIN™, GANCICLOVIR™, FOSCARNET™, CIDOFOVIR™, FLUCONAZOLE™, ITRACONAZOLE™, KETOCONAZOLE™, ACYCLOVIR™, FAMCICLOVIR™, PYRIMETHAMINE™, LEUCOVORIN™, NEUPOGEN™ (filgrastim/G-CSF), and LEUKINE™ (sargramostim/GM-CSF). In a specific embodiment, Therapeutics of the invention are used in any combination with TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, and/or ATOVAQUONE™ to prophylactically treat or prevent an opportunistic *Pneumocystis carinii* pneumonia infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, and/or ETHAMBUTOL™ to prophylactically treat or

prevent an opportunistic *Mycobacterium avium* complex infection. In another specific embodiment, Therapeutics of the invention are used in any combination with RIFABUTIN™, CLARITHROMYCIN™, and/or AZITHROMYCIN™ to prophylactically treat or prevent an opportunistic *Mycobacterium tuberculosis* infection. In another specific embodiment,

5 Therapeutics of the invention are used in any combination with GANCICLOVIR™, FOSCARNET™, and/or CIDOFOVIR™ to prophylactically treat or prevent an opportunistic cytomegalovirus infection. In another specific embodiment, Therapeutics of the invention are used in any combination with FLUCONAZOLE™, ITRACONAZOLE™, and/or KETOCONAZOLE™ to prophylactically treat or prevent an opportunistic fungal infection.

10 In another specific embodiment, Therapeutics of the invention are used in any combination with ACYCLOVIR™ and/or FAMCICOLVIR™ to prophylactically treat or prevent an opportunistic herpes simplex virus type I and/or type II infection. In another specific embodiment, Therapeutics of the invention are used in any combination with PYRIMETHAMINE™ and/or LEUCOVORIN™ to prophylactically treat or prevent an

15 opportunistic *Toxoplasma gondii* infection. In another specific embodiment, Therapeutics of the invention are used in any combination with LEUCOVORIN™ and/or NEUPOGEN™ to prophylactically treat or prevent an opportunistic bacterial infection.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antiviral agent. Antiviral agents that may be administered with the

20 Therapeutics of the invention include, but are not limited to, acyclovir, ribavirin, amantadine, and remantidine.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antibiotic agent. Antibiotic agents that may be administered with the Therapeutics of the invention include, but are not limited to, amoxicillin, beta-lactamases,

25 aminoglycosides, beta-lactam (glycopeptide), beta-lactamases, Clindamycin, chloramphenicol, cephalosporins, ciprofloxacin, ciprofloxacin, erythromycin, fluoroquinolones, macrolides, metronidazole, penicillins, quinolones, rifampin, streptomycin, sulfonamide, tetracyclines, trimethoprim, trimethoprim-sulfamthoxazole, and vancomycin.

Conventional nonspecific immunosuppressive agents, that may be administered in

30 combination with the Therapeutics of the invention include, but are not limited to, steroids, cyclosporine, cyclosporine analogs, cyclophosphamide methylprednisone, prednisone,



azathioprine, FK-506, 15-deoxyspergualin, and other immunosuppressive agents that act by suppressing the function of responding T cells.

In specific embodiments, Therapeutics of the invention are administered in combination with immunosuppressants. Immunosuppressants preparations that may be administered with the Therapeutics of the invention include, but are not limited to, ORTHOCLONE™ (OKT3), SANDIMMUNE™/NEORAL™/SANGDYA™ (cyclosporin), PROGRAF™ (tacrolimus), CELLCEPT™ (mycophenolate), Azathioprine, glucocorticosteroids, and RAPAMUNE™ (sirolimus). In a specific embodiment, immunosuppressants may be used to prevent rejection of organ or bone marrow transplantation.

In an additional embodiment, Therapeutics of the invention are administered alone or in combination with one or more intravenous immune globulin preparations. Intravenous immune globulin preparations that may be administered with the Therapeutics of the invention include, but not limited to, GAMMAR™, IVEEGAM™, SANDOGLOBULIN™, GAMMAGARD S/D™, and GAMIMUNE™. In a specific embodiment, Therapeutics of the invention are administered in combination with intravenous immune globulin preparations in transplantation therapy (e.g., bone marrow transplant).

In an additional embodiment, the Therapeutics of the invention are administered alone or in combination with an anti-inflammatory agent. Anti-inflammatory agents that may be administered with the Therapeutics of the invention include, but are not limited to, glucocorticoids and the nonsteroidal anti-inflammatories, aminoarylcarboxylic acid derivatives, arylacetic acid derivatives, arylbutyric acid derivatives, arylcarboxylic acids, arylpropionic acid derivatives, pyrazoles, pyrazolones, salicylic acid derivatives, thiazinecarboxamides, e-acetamidocaproic acid, S-adenosylmethionine, 3-amino-4-hydroxybutyric acid, amixetrine, bendazac, benzydamine, bucolome, difenpiramide, ditazol, emorfazone, guaiazulene, nabumetone, nimesulide, orgotein, oxaceprol, paranyline, perisoxal, pifoxime, proquazone, proxazole, and tenidap.

In another embodiment, compositions of the invention are administered in combination with a chemotherapeutic agent. Chemotherapeutic agents that may be administered with the Therapeutics of the invention include, but are not limited to, antibiotic derivatives (e.g., doxorubicin, bleomycin, daunorubicin, and dactinomycin); antiestrogens (e.g., tamoxifen); antimetabolites (e.g., fluorouracil, 5-FU, methotrexate, floxuridine, interferon alpha-2b, glutamic acid, plicamycin, mercaptopurine, and 6-thioguanine);

cytotoxic agents (e.g., carmustine, BCNU, lomustine, CCNU, cytosine arabinoside, cyclophosphamide, estramustine, hydroxyurea, procarbazine, mitomycin, busulfan, cis-platin, and vincristine sulfate); hormones (e.g., medroxyprogesterone, estramustine phosphate sodium, ethinyl estradiol, estradiol, megestrol acetate, methyltestosterone, diethylstilbestrol  
5 diphosphate, chlorotrianisene, and testolactone); nitrogen mustard derivatives (e.g., mephallen, chorambucil, mechlorethamine (nitrogen mustard) and thiotepa); steroids and combinations (e.g., bethamethasone sodium phosphate); and others (e.g., dicarbazine, asparaginase, mitotane, vincristine sulfate, vinblastine sulfate, and etoposide).

In a specific embodiment, Therapeutics of the invention are administered in  
10 combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or any combination of the components of CHOP. In another embodiment, Therapeutics of the invention are administered in combination with Rituximab. In a further embodiment, Therapeutics of the invention are administered with Rituxmab and CHOP, or Rituxmab and any combination of the components of CHOP.

15 In an additional embodiment, the Therapeutics of the invention are administered in combination with cytokines. Cytokines that may be administered with the Therapeutics of the invention include, but are not limited to, IL2, IL3, IL4, IL5, IL6, IL7, IL10, IL12, IL13, IL15, anti-CD40, CD40L, IFN-gamma and TNF-alpha. In another embodiment, Therapeutics of the invention may be administered with any interleukin, including, but not  
20 limited to, IL-1alpha, IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, and IL-21.

In an additional embodiment, the Therapeutics of the invention are administered in combination with angiogenic proteins. Angiogenic proteins that may be administered with the Therapeutics of the invention include, but are not limited to, Glioma Derived Growth  
25 Factor (GDGF), as disclosed in European Patent Number EP-399816; Platelet Derived Growth Factor-A (PDGF-A), as disclosed in European Patent Number EP-682110; Platelet Derived Growth Factor-B (PDGF-B), as disclosed in European Patent Number EP-282317; Placental Growth Factor (PlGF), as disclosed in International Publication Number WO 92/06194; Placental Growth Factor-2 (PlGF-2), as disclosed in Hauser et al., Growth Factors,  
30 4:259-268 (1993); Vascular Endothelial Growth Factor (VEGF), as disclosed in International Publication Number WO 90/13649; Vascular Endothelial Growth Factor-A (VEGF-A), as disclosed in European Patent Number EP-506477; Vascular Endothelial Growth Factor-2

(VEGF-2), as disclosed in International Publication Number WO 96/39515; Vascular Endothelial Growth Factor B (VEGF-3); Vascular Endothelial Growth Factor B-186 (VEGF-B186), as disclosed in International Publication Number WO 96/26736; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/02543; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/07832; and Vascular Endothelial Growth Factor-E (VEGF-E), as disclosed in German Patent Number DE19639601. The above mentioned references are incorporated herein by reference herein.

In an additional embodiment, the Therapeutics of the invention are administered in combination with hematopoietic growth factors. Hematopoietic growth factors that may be administered with the Therapeutics of the invention include, but are not limited to, LEUKINE™ (SARGRAMOSTIM™) and NEUPOGEN™ (FILGRASTIM™).

In an additional embodiment, the Therapeutics of the invention are administered in combination with Fibroblast Growth Factors. Fibroblast Growth Factors that may be administered with the Therapeutics of the invention include, but are not limited to, FGF-1, FGF-2, FGF-3, FGF-4, FGF-5, FGF-6, FGF-7, FGF-8, FGF-9, FGF-10, FGF-11, FGF-12, FGF-13, FGF-14, and FGF-15.

In additional embodiments, the Therapeutics of the invention are administered in combination with other therapeutic or prophylactic regimens, such as, for example, radiation therapy.

*Example 14: Method of Treating Decreased Levels of the Polypeptide*

The present invention relates to a method for treating an individual in need of an increased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of an agonist of the invention (including polypeptides of the invention). Moreover, it will be appreciated that conditions caused by a decrease in the standard or normal expression level of a polypeptide of the present invention in an individual can be treated by administering the agonist or antagonist of the present invention. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a Therapeutic comprising an amount of the agonist or

antagonist to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the agonist or antagonist for six consecutive days. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 13.

5

*Example 15: Method of Treating Increased Levels of the Polypeptide*

The present invention also relates to a method of treating an individual in need of a decreased level of a polypeptide of the invention in the body comprising administering to  
10 such an individual a composition comprising a therapeutically effective amount of an antagonist of the invention (including polypeptides and antibodies of the invention).

In one example, antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, due to a variety of etiologies, such as cancer.

15 For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 13.

20 *Example 16: Method of Treatment Using Gene Therapy-Ex Vivo*

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces.  
25 Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated  
30 at 37 degree C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer

is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on  
5 agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1 using primers and having appropriate restriction sites and initiation/stop codons, if necessary. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a  
10 HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the  
15 gene of interest properly inserted.

The amphotropic pA317 or GP+aml2 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce  
20 infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer  
25 cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his.  
30 Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after

having been grown to confluence on cytodex 3 microcarrier beads.

*Example 17: Gene Therapy Using Endogenous Genes Corresponding To Polynucleotides of the Invention*

5

Another method of gene therapy according to the present invention involves operably associating the endogenous polynucleotide sequence of the invention with a promoter via homologous recombination as described, for example, in U.S. Patent NO: 5,641,670, issued June 24, 1997; International Publication NO: WO 96/29411, published September 26, 1996; 10 International Publication NO: WO 94/12650, published August 4, 1994; Koller et al., *Proc. Natl. Acad. Sci. USA*, 86:8932-8935 (1989); and Zijlstra et al., *Nature*, 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made which contain a promoter and targeting 15 sequences, which are homologous to the 5' non-coding sequence of endogenous polynucleotide sequence, flanking the promoter. The targeting sequence will be sufficiently near the 5' end of the polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination. The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct 20 restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter.

The amplified promoter and the amplified targeting sequences are digested with the 25 appropriate restriction enzymes and subsequently treated with calf intestinal phosphatase. The digested promoter and digested targeting sequences are added together in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The construct is size fractionated on an agarose gel then purified by phenol extraction and ethanol precipitation.

30 In this Example, the polynucleotide constructs are administered as naked polynucleotides via electroporation. However, the polynucleotide constructs may also be administered with transfection-facilitating agents, such as liposomes, viral sequences, viral

particles, precipitating agents, etc. Such methods of delivery are known in the art.

Once the cells are transfected, homologous recombination will take place which results in the promoter being operably linked to the endogenous polynucleotide sequence. This results in the expression of polynucleotide corresponding to the polynucleotide in the cell. Expression may be detected by immunological staining, or any other method known in the art.

Fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in DMEM + 10% fetal calf serum. Exponentially growing or early stationary phase fibroblasts are trypsinized and rinsed from the plastic surface with nutrient medium. An aliquot of the cell suspension is removed for counting, and the remaining cells are subjected to centrifugation. The supernatant is aspirated and the pellet is resuspended in 5 ml of electroporation buffer (20 mM HEPES pH 7.3, 137 mM NaCl, 5 mM KCl, 0.7 mM Na<sub>2</sub>HPO<sub>4</sub>, 6 mM dextrose). The cells are recentrifuged, the supernatant aspirated, and the cells resuspended in electroporation buffer containing 1 mg/ml acetylated bovine serum albumin. The final cell suspension contains approximately  $3 \times 10^6$  cells/ml. Electroporation should be performed immediately following resuspension.

Plasmid DNA is prepared according to standard techniques. For example, to construct a plasmid for targeting to the locus corresponding to the polynucleotide of the invention, plasmid pUC18 (MBI Fermentas, Amherst, NY) is digested with HindIII. The CMV promoter is amplified by PCR with an XbaI site on the 5' end and a BamHI site on the 3' end. Two non-coding sequences are amplified via PCR: one non-coding sequence (fragment 1) is amplified with a HindIII site at the 5' end and an Xba site at the 3' end; the other non-coding sequence (fragment 2) is amplified with a BamHI site at the 5' end and a HindIII site at the 3' end. The CMV promoter and the fragments (1 and 2) are digested with the appropriate enzymes (CMV promoter - XbaI and BamHI; fragment 1 - XbaI; fragment 2 - BamHI) and ligated together. The resulting ligation product is digested with HindIII, and ligated with the HindIII-digested pUC18 plasmid.

Plasmid DNA is added to a sterile cuvette with a 0.4 cm electrode gap (Bio-Rad). The final DNA concentration is generally at least 120 µg/ml. 0.5 ml of the cell suspension (containing approximately  $1.5 \times 10^6$  cells) is then added to the cuvette, and the cell suspension and DNA solutions are gently mixed. Electroporation is performed with a Gene-Pulser apparatus (Bio-Rad). Capacitance and voltage are set at 960 µF and 250-300 V,

respectively. As voltage increases, cell survival decreases, but the percentage of surviving cells that stably incorporate the introduced DNA into their genome increases dramatically. Given these parameters, a pulse time of approximately 14-20 mSec should be observed.

Electroporated cells are maintained at room temperature for approximately 5 min, and  
5 the contents of the cuvette are then gently removed with a sterile transfer pipette. The cells are added directly to 10 ml of prewarmed nutrient media (DMEM with 15% calf serum) in a 10 cm dish and incubated at 37 degree C. The following day, the media is aspirated and replaced with 10 ml of fresh media and incubated for a further 16-24 hours.

The engineered fibroblasts are then injected into the host, either alone or after having  
10 been grown to confluence on cytodex 3 microcarrier beads. The fibroblasts now produce the protein product. The fibroblasts can then be introduced into a patient as described above.

*Example 18: Method of Treatment Using Gene Therapy - In Vivo*

15 Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide. The polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary  
20 for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata et al., Cardiovasc. Res. 35(3):470-479 (1997); Chao et al., Pharmacol. Res. 35(6):517-522 (1997); Wolff, Neuromuscul. Disord. 7(5):314-318 (1997); Schwartz et al., Gene Ther. 3(5):405-411 (1996); Tsurumi et al.,  
25 Circulation 94(12):3281-3290 (1996) (incorporated herein by reference).

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

30 The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell,



including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) Ann. NY Acad. Sci. 772:126-139 and Abdallah B. et al. (1995) Biol. Cell 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will

appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

#### *Example 19: Transgenic Animals*

The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, *e.g.*, baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (*i.e.*, polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40:691-698 (1994); Carver et al., Biotechnology (NY) 11:1263-1270 (1993); Wright et al., Biotechnology (NY) 9:830-834 (1991); and Hoppe et al., U.S. Pat. No. 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82:6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56:313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3:1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, *e.g.*, Ulmer et al., Science 259:1745 (1993); introducing nucleic acid constructs into embryonic pluripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (Lavitrano et al., Cell 57:717-723 (1989); etc. For a review of such techniques, see Gordon, "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989), which is incorporated by reference herein in its entirety.

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., Nature 380:64-66 (1996); Wilmut et al., Nature 385:810-813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, *i.e.*, mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, *e.g.*, head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci.

USA 89:6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265:103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, *in situ* hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

5

*Example 20: Knock-Out Animals*

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (*E.g.*, see Smithies et al., *Nature* 317:230-234 (1985); Thomas & Capecchi, *Cell* 51:503-512 (1987); Thompson et al., *Cell* 5:313-321 (1989); each of which is incorporated by reference herein in its entirety). For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention *in vivo*. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (*e.g.*, see Thomas & Capecchi 1987 and Thompson 1989, *supra*). However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site *in vivo* using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (*e.g.*, knockouts) are administered to a patient *in vivo*. Such cells may be obtained from the patient (*i.e.*, animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (*e.g.*, lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered *in vitro* using recombinant DNA techniques to introduce the coding

30

sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc. The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e.g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, e.g., genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U.S. Patent No. 5,399,349; and Mulligan & Wilson, U.S. Patent No. 5,460,959 each of which is incorporated by reference herein in its entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

*Example 22: Assays Detecting Stimulation or Inhibition of B cell Proliferation and Differentiation*

30

Generation of functional humoral immune responses requires both soluble and cognate signaling between B-lineage cells and their microenvironment. Signals may impart a

positive stimulus that allows a B-lineage cell to continue its programmed development, or a negative stimulus that instructs the cell to arrest its current developmental pathway. To date, numerous stimulatory and inhibitory signals have been found to influence B cell responsiveness including IL-2, IL-4, IL-5, IL-6, IL-7, IL-10, IL-13, IL-14 and IL-15.

5 Interestingly, these signals are by themselves weak effectors but can, in combination with various co-stimulatory proteins, induce activation, proliferation, differentiation, homing, tolerance and death among B cell populations.

One of the best studied classes of B-cell co-stimulatory proteins is the TNF-superfamily. Within this family CD40, CD27, and CD30 along with their respective ligands CD154, CD70, and CD153 have been found to regulate a variety of immune responses. Assays which allow for the detection and/or observation of the proliferation and differentiation of these B-cell populations and their precursors are valuable tools in determining the effects various proteins may have on these B-cell populations in terms of proliferation and differentiation. Listed below are two assays designed to allow for the  
15 detection of the differentiation, proliferation, or inhibition of B-cell populations and their precursors.

**In Vitro Assay-** Agonists or antagonists of the invention can be assessed for its ability to induce activation, proliferation, differentiation or inhibition and/or death in B-cell populations and their precursors. The activity of the agonists or antagonists of the invention  
20 on purified human tonsillar B cells, measured qualitatively over the dose range from 0.1 to 10,000 ng/mL, is assessed in a standard B-lymphocyte co-stimulation assay in which purified tonsillar B cells are cultured in the presence of either formalin-fixed *Staphylococcus aureus* Cowan I (SAC) or immobilized anti-human IgM antibody as the priming agent. Second signals such as IL-2 and IL-15 synergize with SAC and IgM crosslinking to elicit B cell  
25 proliferation as measured by tritiated-thymidine incorporation. Novel synergizing agents can be readily identified using this assay. The assay involves isolating human tonsillar B cells by magnetic bead (MACS) depletion of CD3-positive cells. The resulting cell population is greater than 95% B cells as assessed by expression of CD45R(B220).

Various dilutions of each sample are placed into individual wells of a 96-well plate to  
30 which are added  $10^5$  B-cells suspended in culture medium (RPMI 1640 containing 10% FBS,  $5 \times 10^{-5}$ M 2ME, 100U/ml penicillin, 10ug/ml streptomycin, and  $10^{-5}$  dilution of SAC) in a total volume of 150ul. Proliferation or inhibition is quantitated by a 20h pulse (1uCi/well)

with 3H-thymidine (6.7 Ci/mM) beginning 72h post factor addition. The positive and negative controls are IL2 and medium respectively.

**In Vivo Assay-** BALB/c mice are injected (i.p.) twice per day with buffer only, or 2 mg/Kg of agonists or antagonists of the invention, or truncated forms thereof. Mice receive this treatment for 4 consecutive days, at which time they are sacrificed and various tissues and serum collected for analyses. Comparison of H&E sections from normal spleens and spleens treated with agonists or antagonists of the invention identify the results of the activity of the agonists or antagonists on spleen cells, such as the diffusion of peri-arterial lymphatic sheaths, and/or significant increases in the nucleated cellularity of the red pulp regions, which may indicate the activation of the differentiation and proliferation of B-cell populations. Immunohistochemical studies using a B cell marker, anti-CD45R(B220), are used to determine whether any physiological changes to splenic cells, such as splenic disorganization, are due to increased B-cell representation within loosely defined B-cell zones that infiltrate established T-cell regions.

Flow cytometric analyses of the spleens from mice treated with agonist or antagonist is used to indicate whether the agonists or antagonists specifically increases the proportion of ThB+, CD45R(B220)dull B cells over that which is observed in control mice. Likewise, a predicted consequence of increased mature B-cell representation in vivo is a relative increase in serum Ig titers. Accordingly, serum IgM and IgA levels are compared between buffer and agonists or antagonists-treated mice.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

#### *Example 23: T Cell Proliferation Assay*

A CD3-induced proliferation assay is performed on PBMCs and is measured by the uptake of <sup>3</sup>H-thymidine. The assay is performed as follows. Ninety-six well plates are coated with 100 µl/well of mAb to CD3 (HIT3a, Pharmingen) or isotype-matched control mAb (B33.1) overnight at 4 degrees C (1 µg/ml in .05M bicarbonate buffer, pH 9.5), then washed three times with PBS. PBMC are isolated by F/H gradient centrifugation from human peripheral blood and added to quadruplicate wells (5 x 10<sup>4</sup>/well) of mAb coated plates



in RPMI containing 10% FCS and P/S in the presence of varying concentrations of agonists or antagonists of the invention (total volume 200  $\mu$ l). Relevant protein buffer and medium alone are controls. After 48 hr. culture at 37 degrees C, plates are spun for 2 min. at 1000 rpm and 100  $\mu$ l of supernatant is removed and stored -20 degrees C for measurement of IL-2 (or other cytokines) if effect on proliferation is observed. Wells are supplemented with 100  $\mu$ l of medium containing 0.5  $\mu$ Ci of  $^3$ H-thymidine and cultured at 37 degrees C for 18-24 hr. Wells are harvested and incorporation of  $^3$ H-thymidine used as a measure of proliferation. Anti-CD3 alone is the positive control for proliferation. IL-2 (100 U/ml) is also used as a control which enhances proliferation. Control antibody which does not induce proliferation of T cells is used as the negative controls for the effects of agonists or antagonists of the invention.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

*Example 24: Effect of Agonists or Antagonists of the Invention on the Expression of MHC Class II, Costimulatory and Adhesion Molecules and Cell Differentiation of Monocytes and Monocyte-Derived Human Dendritic Cells*

Dendritic cells are generated by the expansion of proliferating precursors found in the peripheral blood: adherent PBMC or elutriated monocytic fractions are cultured for 7-10 days with GM-CSF (50 ng/ml) and IL-4 (20 ng/ml). These dendritic cells have the characteristic phenotype of immature cells (expression of CD1, CD80, CD86, CD40 and MHC class II antigens). Treatment with activating factors, such as TNF- $\alpha$ , causes a rapid change in surface phenotype (increased expression of MHC class I and II, costimulatory and adhesion molecules, downregulation of FC $\gamma$ RII, upregulation of CD83). These changes correlate with increased antigen-presenting capacity and with functional maturation of the dendritic cells.

FACS analysis of surface antigens is performed as follows. Cells are treated 1-3 days with increasing concentrations of agonist or antagonist of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degrees C. After an additional wash, the labeled cells are analyzed by flow

cytometry on a FACScan (Becton Dickinson).

Effect on the production of cytokines. Cytokines generated by dendritic cells, in particular IL-12, are important in the initiation of T-cell dependent immune responses. IL-12 strongly influences the development of Th1 helper T-cell immune response, and induces cytotoxic T and NK cell function. An ELISA is used to measure the IL-12 release as follows. Dendritic cells ( $10^6$ /ml) are treated with increasing concentrations of agonists or antagonists of the invention for 24 hours. LPS (100 ng/ml) is added to the cell culture as positive control. Supernatants from the cell cultures are then collected and analyzed for IL-12 content using commercial ELISA kit (e.g., R & D Systems (Minneapolis, MN)). The standard protocols provided with the kits are used.

Effect on the expression of MHC Class II, costimulatory and adhesion molecules. Three major families of cell surface antigens can be identified on monocytes: adhesion molecules, molecules involved in antigen presentation, and Fc receptor. Modulation of the expression of MHC class II antigens and other costimulatory molecules, such as B7 and ICAM-1, may result in changes in the antigen presenting capacity of monocytes and ability to induce T cell activation. Increase expression of Fc receptors may correlate with improved monocyte cytotoxic activity, cytokine release and phagocytosis.

FACS analysis is used to examine the surface antigens as follows. Monocytes are treated 1-5 days with increasing concentrations of agonists or antagonists of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degreesC. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

Monocyte activation and/or increased survival. Assays for molecules that activate (or alternatively, inactivate) monocytes and/or increase monocyte survival (or alternatively, decrease monocyte survival) are known in the art and may routinely be applied to determine whether a molecule of the invention functions as an inhibitor or activator of monocytes. Agonists or antagonists of the invention can be screened using the three assays described below. For each of these assays, Peripheral blood mononuclear cells (PBMC) are purified

from single donor leukopacks (American Red Cross, Baltimore, MD) by centrifugation through a Histopaque gradient (Sigma). Monocytes are isolated from PBMC by counterflow centrifugal elutriation.

- 5 Monocyte Survival Assay. Human peripheral blood monocytes progressively lose viability when cultured in absence of serum or other stimuli. Their death results from internally regulated process (apoptosis). Addition to the culture of activating factors, such as TNF-alpha dramatically improves cell survival and prevents DNA fragmentation. Propidium iodide (PI) staining is used to measure apoptosis as follows. Monocytes are cultured for 48 hours in  
10 polypropylene tubes in serum-free medium (positive control), in the presence of 100 ng/ml TNF-alpha (negative control), and in the presence of varying concentrations of the compound to be tested. Cells are suspended at a concentration of  $2 \times 10^6$ /ml in PBS containing PI at a final concentration of 5  $\mu$ g/ml, and then incubated at room temperature for 5 minutes before FACScan analysis. PI uptake has been demonstrated to correlate with DNA fragmentation in  
15 this experimental paradigm.

Effect on cytokine release. An important function of monocytes/macrophages is their regulatory activity on other cellular populations of the immune system through the release of cytokines after stimulation. An ELISA to measure cytokine release is performed as follows.

- 20 Human monocytes are incubated at a density of  $5 \times 10^5$  cells/ml with increasing concentrations of agonists or antagonists of the invention and under the same conditions, but in the absence of agonists or antagonists. For IL-12 production, the cells are primed overnight with IFN (100 U/ml) in presence of agonist or antagonist of the invention. LPS (10 ng/ml) is then added. Conditioned media are collected after 24h and kept frozen until use.  
25 Measurement of TNF-alpha, IL-10, MCP-1 and IL-8 is then performed using a commercially available ELISA kit (e. g, R & D Systems (Minneapolis, MN)) and applying the standard protocols provided with the kit.

- Oxidative burst. Purified monocytes are plated in 96-w plate at  $2 \times 10^5$  cell/well. Increasing  
30 concentrations of agonists or antagonists of the invention are added to the wells in a total volume of 0.2 ml culture medium (RPMI 1640 + 10% FCS, glutamine and antibiotics). After 3 days incubation, the plates are centrifuged and the medium is removed from the wells. To

the macrophage monolayers, 0.2 ml per well of phenol red solution (140 mM NaCl, 10 mM potassium phosphate buffer pH 7.0, 5.5 mM dextrose, 0.56 mM phenol red and 19 U/ml of HRPO) is added, together with the stimulant (200 nM PMA). The plates are incubated at 37°C for 2 hours and the reaction is stopped by adding 20 µl 1N NaOH per well. The  
5 absorbance is read at 610 nm. To calculate the amount of H<sub>2</sub>O<sub>2</sub> produced by the macrophages, a standard curve of a H<sub>2</sub>O<sub>2</sub> solution of known molarity is performed for each experiment.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test  
10 the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

*Example 25: Biological Effects of Agonists or Antagonists of the Invention*

15 Astrocyte and Neuronal Assays.

Agonists or antagonists of the invention, expressed in *Escherichia coli* and purified as described above, can be tested for activity in promoting the survival, neurite outgrowth, or phenotypic differentiation of cortical neuronal cells and for inducing the proliferation of glial fibrillary acidic protein immunopositive cells, astrocytes. The selection of cortical cells for  
20 the bioassay is based on the prevalent expression of FGF-1 and FGF-2 in cortical structures and on the previously reported enhancement of cortical neuronal survival resulting from FGF-2 treatment. A thymidine incorporation assay, for example, can be used to elucidate an agonist or antagonist of the invention's activity on these cells.

Moreover, previous reports describing the biological effects of FGF-2 (basic FGF) on  
25 cortical or hippocampal neurons *in vitro* have demonstrated increases in both neuron survival and neurite outgrowth (Walicke et al., "Fibroblast growth factor promotes survival of dissociated hippocampal neurons and enhances neurite extension." *Proc. Natl. Acad. Sci. USA* 83:3012-3016. (1986), assay herein incorporated by reference in its entirety). However, reports from experiments done on PC-12 cells suggest that these two responses are not  
30 necessarily synonymous and may depend on not only which FGF is being tested but also on which receptor(s) are expressed on the target cells. Using the primary cortical neuronal

culture paradigm, the ability of an agonist or antagonist of the invention to induce neurite outgrowth can be compared to the response achieved with FGF-2 using, for example, a thymidine incorporation assay.

5 Fibroblast and endothelial cell assays.

Human lung fibroblasts are obtained from Clonetics (San Diego, CA) and maintained in growth media from Clonetics. Dermal microvascular endothelial cells are obtained from Cell Applications (San Diego, CA). For proliferation assays, the human lung fibroblasts and dermal microvascular endothelial cells can be cultured at 5,000 cells/well in a 96-well plate  
10 for one day in growth medium. The cells are then incubated for one day in 0.1% BSA basal medium. After replacing the medium with fresh 0.1% BSA medium, the cells are incubated with the test proteins for 3 days. Alamar Blue (Alamar Biosciences, Sacramento, CA) is added to each well to a final concentration of 10%. The cells are incubated for 4 hr. Cell viability is measured by reading in a CytoFluor fluorescence reader. For the PGE<sub>2</sub> assays,  
15 the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or agonists or antagonists of the invention with or without IL-1 $\alpha$  for 24 hours. The supernatants are collected and assayed for PGE<sub>2</sub> by EIA kit (Cayman, Ann Arbor, MI). For the IL-6 assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one  
20 day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or with or without agonists or antagonists of the invention IL-1 $\alpha$  for 24 hours. The supernatants are collected and assayed for IL-6 by ELISA kit (Endogen, Cambridge, MA).

Human lung fibroblasts are cultured with FGF-2 or agonists or antagonists of the invention for 3 days in basal medium before the addition of Alamar Blue to assess effects on  
25 growth of the fibroblasts. FGF-2 should show a stimulation at 10 - 2500 ng/ml which can be used to compare stimulation with agonists or antagonists of the invention.

Parkinson Models.

The loss of motor function in Parkinson's disease is attributed to a deficiency of  
30 striatal dopamine resulting from the degeneration of the nigrostriatal dopaminergic projection

neurons. An animal model for Parkinson's that has been extensively characterized involves the systemic administration of 1-methyl-4 phenyl 1,2,3,6-tetrahydropyridine (MPTP). In the CNS, MPTP is taken-up by astrocytes and catabolized by monoamine oxidase B to 1-methyl-4-phenyl pyridine (MPP<sup>+</sup>) and released. Subsequently, MPP<sup>+</sup> is actively accumulated in  
5 dopaminergic neurons by the high-affinity reuptake transporter for dopamine. MPP<sup>+</sup> is then concentrated in mitochondria by the electrochemical gradient and selectively inhibits nicotinamide adenine disphosphate: ubiquinone oxidoreductionase (complex I), thereby interfering with electron transport and eventually generating oxygen radicals.

It has been demonstrated in tissue culture paradigms that FGF-2 (basic FGF) has  
10 trophic activity towards nigral dopaminergic neurons (Ferrari et al., Dev. Biol. 1989). Recently, Dr. Unsicker's group has demonstrated that administering FGF-2 in gel foam implants in the striatum results in the near complete protection of nigral dopaminergic neurons from the toxicity associated with MPTP exposure (Otto and Unsicker, J. Neuroscience, 1990).

15 Based on the data with FGF-2, agonists or antagonists of the invention can be evaluated to determine whether it has an action similar to that of FGF-2 in enhancing dopaminergic neuronal survival *in vitro* and it can also be tested *in vivo* for protection of dopaminergic neurons in the striatum from the damage associated with MPTP treatment. The potential effect of an agonist or antagonist of the invention is first examined *in vitro* in a  
20 dopaminergic neuronal cell culture paradigm. The cultures are prepared by dissecting the midbrain floor plate from gestation day 14 Wistar rat embryos. The tissue is dissociated with trypsin and seeded at a density of 200,000 cells/cm<sup>2</sup> on polyorthinine-laminin coated glass coverslips. The cells are maintained in Dulbecco's Modified Eagle's medium and F12 medium containing hormonal supplements (N1). The cultures are fixed with  
25 paraformaldehyde after 8 days *in vitro* and are processed for tyrosine hydroxylase, a specific marker for dopaminergic neurons, immunohistochemical staining. Dissociated cell cultures are prepared from embryonic rats. The culture medium is changed every third day and the factors are also added at that time.

Since the dopaminergic neurons are isolated from animals at gestation day 14, a  
30 developmental time which is past the stage when the dopaminergic precursor cells are proliferating, an increase in the number of tyrosine hydroxylase immunopositive neurons would represent an increase in the number of dopaminergic neurons surviving *in vitro*.

Therefore, if an agonist or antagonist of the invention acts to prolong the survival of dopaminergic neurons, it would suggest that the agonist or antagonist may be involved in Parkinson's Disease.

5 The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

10 *Example 26: The Effect of Agonists or Antagonists of the Invention on the Growth of Vascular Endothelial Cells*

On day 1, human umbilical vein endothelial cells (HUVEC) are seeded at  $2.5 \times 10^4$  cells/35 mm dish density in M199 medium containing 4% fetal bovine serum (FBS), 16 units/ml heparin, and 50 units/ml endothelial cell growth supplements (ECGS, Biotechnology, Inc.). On day 2, the medium is replaced with M199 containing 10% FBS, 8 units/ml heparin. An agonist or antagonist of the invention, and positive controls, such as VEGF and basic FGF (bFGF) are added, at varying concentrations. On days 4 and 6, the medium is replaced. On day 8, cell number is determined with a Coulter Counter.

20 An increase in the number of HUVEC cells indicates that the compound of the invention may proliferate vascular endothelial cells, while a decrease in the number of HUVEC cell indicates that the compound of the invention inhibits vascular endothelial cells.

The studies described in this example tested activity of a polypeptide of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), agonists, and/or antagonists of the invention.

25

*Example 27: Rat Corneal Wound Healing Model*

This animal model shows the effect of an agonist or antagonist of the invention on neovascularization. The experimental protocol includes:

- 30 a) Making a 1-1.5 mm long incision from the center of cornea into the stromal layer.
- b) Inserting a spatula below the lip of the incision facing the outer corner of the

eye.

c) Making a pocket (its base is 1-1.5 mm from the edge of the eye).

d) Positioning a pellet, containing 50ng- 5ug of an agonist or antagonist of the invention, within the pocket.

5 e) Treatment with an agonist or antagonist of the invention can also be applied topically to the corneal wounds in a dosage range of 20mg - 500mg (daily treatment for five days).

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test  
10 the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

*Example 28: Diabetic Mouse and Glucocorticoid-Impaired Wound Healing Models*

*A. Diabetic db+/db+ Mouse Model.*

15 To demonstrate that an agonist or antagonist of the invention accelerates the healing process, the genetically diabetic mouse model of wound healing is used. The full thickness wound healing model in the db+/db+ mouse is a well characterized, clinically relevant and reproducible model of impaired wound healing. Healing of the diabetic wound is dependent on formation of granulation tissue and re-epithelialization rather than contraction (Gartner,  
20 M.H. *et al.*, *J. Surg. Res.* 52:389 (1992); Greenhalgh, D.G. *et al.*, *Am. J. Pathol.* 136:1235 (1990)).

The diabetic animals have many of the characteristic features observed in Type II diabetes mellitus. Homozygous (db+/db+) mice are obese in comparison to their normal heterozygous (db+/+m) littermates. Mutant diabetic (db+/db+) mice have a single autosomal  
25 recessive mutation on chromosome 4 (db+) (Coleman *et al.* *Proc. Natl. Acad. Sci. USA* 77:283-293 (1982)). Animals show polyphagia, polydipsia and polyuria. Mutant diabetic mice (db+/db+) have elevated blood glucose, increased or normal insulin levels, and suppressed cell-mediated immunity (Mandel *et al.*, *J. Immunol.* 120:1375 (1978); Debray-Sachs, M. *et al.*, *Clin. Exp. Immunol.* 51(1):1-7 (1983); Leiter *et al.*, *Am. J. of Pathol.* 114:46-  
30 55 (1985)). Peripheral neuropathy, myocardial complications, and microvascular lesions, basement membrane thickening and glomerular filtration abnormalities have been described in these animals (Norido, F. *et al.*, *Exp. Neurol.* 83(2):221-232 (1984); Robertson *et al.*,



*Diabetes* 29(1):60-67 (1980); Giacomelli *et al.*, *Lab Invest.* 40(4):460-473 (1979); Coleman, D.L., *Diabetes* 31 (Suppl):1-6 (1982)). These homozygous diabetic mice develop hyperglycemia that is resistant to insulin analogous to human type II diabetes (Mandel *et al.*, *J. Immunol.* 120:1375-1377 (1978)).

5       The characteristics observed in these animals suggests that healing in this model may be similar to the healing observed in human diabetes (Greenhalgh, *et al.*, *Am. J. of Pathol.* 136:1235-1246 (1990)).

Genetically diabetic female C57BL/KsJ (db+/db+) mice and their non-diabetic (db+/+m) heterozygous littermates are used in this study (Jackson Laboratories). The  
10   animals are purchased at 6 weeks of age and are 8 weeks old at the beginning of the study. Animals are individually housed and received food and water ad libitum. All manipulations are performed using aseptic techniques. The experiments are conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

15       Wounding protocol is performed according to previously reported methods (Tsuboi, R. and Rifkin, D.B., *J. Exp. Med.* 172:245-251 (1990)). Briefly, on the day of wounding, animals are anesthetized with an intraperitoneal injection of Avertin (0.01 mg/mL), 2,2,2-tribromoethanol and 2-methyl-2-butanol dissolved in deionized water. The dorsal region of the animal is shaved and the skin washed with 70% ethanol solution and iodine. The surgical  
20   area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is then created using a Keyes tissue punch. Immediately following wounding, the surrounding skin is gently stretched to eliminate wound expansion. The wounds are left open for the duration of the experiment. Application of the treatment is given topically for 5 consecutive days commencing on the day of wounding. Prior to treatment, wounds are gently cleansed with  
25   sterile saline and gauze sponges.

Wounds are visually examined and photographed at a fixed distance at the day of surgery and at two day intervals thereafter. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no  
30   longer visible and the wound is covered by a continuous epithelium.

An agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups

received 50mL of vehicle solution.

Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology and immunohistochemistry. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

Three groups of 10 animals each (5 diabetic and 5 non-diabetic controls) are evaluated: 1) Vehicle placebo control, 2) untreated group, and 3) treated group.

Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total square area of the wound. Contraction is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm<sup>2</sup>, the corresponding size of the dermal punch. Calculations are made using the following formula:

$$[\text{Open area on day 8}] - [\text{Open area on day 1}] / [\text{Open area on day 1}]$$

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using a Reichert-Jung microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds are used to assess whether the healing process and the morphologic appearance of the repaired skin is altered by treatment with an agonist or antagonist of the invention. This assessment included verification of the presence of cell accumulation, inflammatory cells, capillaries, fibroblasts, re-epithelialization and epidermal maturity (Greenhalgh, D.G. *et al.*, *Am. J. Pathol.* 136:1235 (1990)). A calibrated lens micrometer is used by a blinded observer.

Tissue sections are also stained immunohistochemically with a polyclonal rabbit anti-human keratin antibody using ABC Elite detection system. Human skin is used as a positive tissue control while non-immune IgG is used as a negative control. Keratinocyte growth is determined by evaluating the extent of reepithelialization of the wound using a calibrated lens micrometer.

Proliferating cell nuclear antigen/cyclin (PCNA) in skin specimens is demonstrated by using anti-PCNA antibody (1:50) with an ABC Elite detection system. Human colon cancer served as a positive tissue control and human brain tissue is used as a negative tissue

control. Each specimen included a section with omission of the primary antibody and substitution with non-immune mouse IgG. Ranking of these sections is based on the extent of proliferation on a scale of 0-8, the lower side of the scale reflecting slight proliferation to the higher side reflecting intense proliferation.

- 5 Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

#### *B. Steroid Impaired Rat Model*

- The inhibition of wound healing by steroids has been well documented in various *in vitro* and  
10 *in vivo* systems (Wahl, Glucocorticoids and Wound healing. In: Anti-Inflammatory Steroid Action: Basic and Clinical Aspects. 280-302 (1989); Wahlet *et al.*, *J. Immunol.* 115: 476-481 (1975); Werb *et al.*, *J. Exp. Med.* 147:1684-1694 (1978)). Glucocorticoids retard wound healing by inhibiting angiogenesis, decreasing vascular permeability (Ebert *et al.*, *Am. Intern. Med.* 37:701-705 (1952)), fibroblast proliferation, and collagen synthesis (Beck *et al.*,  
15 *Growth Factors.* 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978)) and producing a transient reduction of circulating monocytes (Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989)). The systemic administration of steroids to impaired wound healing is a well establish  
20 phenomenon in rats (Beck *et al.*, *Growth Factors.* 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989); Pierce *et al.*, *Proc. Natl. Acad. Sci. USA* 86: 2229-2233 (1989)).

- To demonstrate that an agonist or antagonist of the invention can accelerate the  
25 healing process, the effects of multiple topical applications of the agonist or antagonist on full thickness excisional skin wounds in rats in which healing has been impaired by the systemic administration of methylprednisolone is assessed.

- Young adult male Sprague Dawley rats weighing 250-300 g (Charles River Laboratories) are used in this example. The animals are purchased at 8 weeks of age and are  
30 9 weeks old at the beginning of the study. The healing response of rats is impaired by the systemic administration of methylprednisolone (17mg/kg/rat intramuscularly) at the time of wounding. Animals are individually housed and received food and water *ad libitum*. All

manipulations are performed using aseptic techniques. This study is conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

The wounding protocol is followed according to section A, above. On the day of  
5 wounding, animals are anesthetized with an intramuscular injection of ketamine (50 mg/kg) and xylazine (5 mg/kg). The dorsal region of the animal is shaved and the skin washed with 70% ethanol and iodine solutions. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is created using a Keyes tissue punch. The wounds are left open for the duration of the experiment. Applications of the testing materials  
10 are given topically once a day for 7 consecutive days commencing on the day of wounding and subsequent to methylprednisolone administration. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

Wounds are visually examined and photographed at a fixed distance at the day of wounding and at the end of treatment. Wound closure is determined by daily measurement on  
15 days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

The agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups  
20 received 50mL of vehicle solution.

Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

25 Four groups of 10 animals each (5 with methylprednisolone and 5 without glucocorticoid) are evaluated: 1) Untreated group 2) Vehicle placebo control 3) treated groups.

Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total area of the wound. Closure is then estimated by establishing the  
30 differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is  $64\text{mm}^2$ , the corresponding size of the dermal punch. Calculations are made using the following formula:

[Open area on day 8] - [Open area on day 1] / [Open area on day 1]

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned  
5 perpendicular to the wound surface (5mm) and cut using an Olympus microtome. Routine  
hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds.  
Histologic examination of the wounds allows assessment of whether the healing process and  
the morphologic appearance of the repaired skin is improved by treatment with an agonist or  
antagonist of the invention. A calibrated lens micrometer is used by a blinded observer to  
10 determine the distance of the wound gap.

Experimental data are analyzed using an unpaired t test. A p value of  $< 0.05$  is  
considered significant.

The studies described in this example tested activity of agonists or antagonists of the  
invention. However, one skilled in the art could easily modify the exemplified studies to test  
15 the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

#### *Example 29: Lymphedema Animal Model*

The purpose of this experimental approach is to create an appropriate and consistent  
20 lymphedema model for testing the therapeutic effects of an agonist or antagonist of the  
invention in lymphangiogenesis and re-establishment of the lymphatic circulatory system in  
the rat hind limb. Effectiveness is measured by swelling volume of the affected limb,  
quantification of the amount of lymphatic vasculature, total blood plasma protein, and  
histopathology. Acute lymphedema is observed for 7-10 days. Perhaps more importantly,  
25 the chronic progress of the edema is followed for up to 3-4 weeks.

Prior to beginning surgery, blood sample is drawn for protein concentration analysis.  
Male rats weighing approximately ~350g are dosed with Pentobarbital. Subsequently, the  
right legs are shaved from knee to hip. The shaved area is swabbed with gauze soaked in  
70% EtOH. Blood is drawn for serum total protein testing. Circumference and volumetric  
30 measurements are made prior to injecting dye into paws after marking 2 measurement levels  
(0.5 cm above heel, at mid-pt of dorsal paw). The intradermal dorsum of both right and left  
paws are injected with 0.05 ml of 1% Evan's Blue. Circumference and volumetric

measurements are then made following injection of dye into paws.

Using the knee joint as a landmark, a mid-leg inguinal incision is made circumferentially allowing the femoral vessels to be located. Forceps and hemostats are used to dissect and separate the skin flaps. After locating the femoral vessels, the lymphatic vessel  
5 that runs along side and underneath the vessel(s) is located. The main lymphatic vessels in this area are then electrically coagulated or suture ligated.

Using a microscope, muscles in back of the leg (near the semitendinosus and adductors) are bluntly dissected. The popliteal lymph node is then located. The 2 proximal and 2 distal lymphatic vessels and distal blood supply of the popliteal node are then and  
10 ligated by suturing. The popliteal lymph node, and any accompanying adipose tissue, is then removed by cutting connective tissues.

Care is taken to control any mild bleeding resulting from this procedure. After lymphatics are occluded, the skin flaps are sealed by using liquid skin (Vetbond) (AJ Buck). The separated skin edges are sealed to the underlying muscle tissue while leaving a gap of  
15 ~0.5 cm around the leg. Skin also may be anchored by suturing to underlying muscle when necessary.

To avoid infection, animals are housed individually with mesh (no bedding). Recovering animals are checked daily through the optimal edematous peak, which typically occurred by day 5-7. The plateau edematous peak are then observed. To evaluate the  
20 intensity of the lymphedema, the circumference and volumes of 2 designated places on each paw before operation and daily for 7 days are measured. The effect plasma proteins on lymphedema is determined and whether protein analysis is a useful testing perimeter is also investigated. The weights of both control and edematous limbs are evaluated at 2 places. Analysis is performed in a blind manner.

25 Circumference Measurements: Under brief gas anesthetic to prevent limb movement, a cloth tape is used to measure limb circumference. Measurements are done at the ankle bone and dorsal paw by 2 different people then those 2 readings are averaged. Readings are taken from both control and edematous limbs.

Volumetric Measurements: On the day of surgery, animals are anesthetized with  
30 Pentobarbital and are tested prior to surgery. For daily volumetrics animals are under brief halothane anesthetic (rapid immobilization and quick recovery), both legs are shaved and equally marked using waterproof marker on legs. Legs are first dipped in water, then dipped

into instrument to each marked level then measured by Buxco edema software(Chen/Victor). Data is recorded by one person, while the other is dipping the limb to marked area.

Blood-plasma protein measurements: Blood is drawn, spun, and serum separated prior to surgery and then at conclusion for total protein and Ca<sup>2+</sup> comparison.

5       Limb Weight Comparison: After drawing blood, the animal is prepared for tissue collection. The limbs are amputated using a quillitine, then both experimental and control legs are cut at the ligature and weighed. A second weighing is done as the tibio-cacaneal joint is disarticulated and the foot is weighed.

10       Histological Preparations: The transverse muscle located behind the knee (popliteal) area is dissected and arranged in a metal mold, filled with freezeGel, dipped into cold methylbutane, placed into labeled sample bags at - 80EC until sectioning. Upon sectioning, the muscle is observed under fluorescent microscopy for lymphatics..

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test  
15       the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

*Example 30: Suppression of TNF alpha-induced adhesion molecule expression by a Agonist or Antagonist of the Invention*

20       The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial  
25       leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

30       Tumor necrosis factor alpha (TNF-a), a potent proinflammatory cytokine, is a stimulator of all three CAMs on endothelial cells and may be involved in a wide variety of inflammatory responses, often resulting in a pathological outcome.

The potential of an agonist or antagonist of the invention to mediate a suppression of TNF- $\alpha$  induced CAM expression can be examined. A modified ELISA assay which uses ECs as a solid phase absorbent is employed to measure the amount of CAM expression on TNF- $\alpha$  treated ECs when co-stimulated with a member of the FGF family of proteins.

5 To perform the experiment, human umbilical vein endothelial cell (HUVEC) cultures are obtained from pooled cord harvests and maintained in growth medium (EGM-2; Clonetics, San Diego, CA) supplemented with 10% FCS and 1% penicillin/streptomycin in a 37 degree C humidified incubator containing 5% CO<sub>2</sub>. HUVECs are seeded in 96-well plates at concentrations of  $1 \times 10^4$  cells/well in EGM medium at 37 degree C for 18-24 hrs or  
10 until confluent. The monolayers are subsequently washed 3 times with a serum-free solution of RPMI-1640 supplemented with 100 U/ml penicillin and 100 mg/ml streptomycin, and treated with a given cytokine and/or growth factor(s) for 24 h at 37 degree C. Following incubation, the cells are then evaluated for CAM expression.

Human Umbilical Vein Endothelial cells (HUVECs) are grown in a standard 96 well  
15 plate to confluence. Growth medium is removed from the cells and replaced with 90  $\mu$ l of 199 Medium (10% FBS). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10  $\mu$ l volumes). Plates are incubated at 37 degree C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100  $\mu$ l of 0.1% paraformaldehyde-PBS(with Ca<sup>++</sup> and Mg<sup>++</sup>) is added  
20 to each well. Plates are held at 4°C for 30 min.

Fixative is then removed from the wells and wells are washed 1X with PBS(+Ca,Mg)+0.5% BSA and drained. Do not allow the wells to dry. Add 10  $\mu$ l of diluted primary antibody to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10  $\mu$ g/ml (1:10 dilution of 0.1  
25 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA.

Then add 20  $\mu$ l of diluted ExtrAvidin-Alkaline Phosphatase (1:5,000 dilution) to each well and incubated at 37°C for 30 min. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA. 1 tablet of p-Nitrophenol Phosphate pNPP is dissolved in 5 ml of glycine buffer (pH  
30 10.4). 100  $\mu$ l of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphatase in glycine buffer:  $1:5,000 (10^0) > 10^{-0.5} > 10^{-1} > 10^{-1.5}$ . 5  $\mu$ l of each dilution is added to triplicate



wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100  $\mu$ l of pNPN reagent must then be added to each of the standard wells. The plate must be incubated at 37°C for 4h. A volume of 50  $\mu$ l of 3M NaOH is added to all wells. The results are quantified on a plate reader at 405 nm. The background subtraction option is used on  
5 blank wells filled with glycine buffer only. The template is set up to indicate the concentration of AP-conjugate in each standard well [ 5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test  
10 the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

*Example 31: Production Of Polypeptide of the Invention For High-Throughput Screening Assays*

15 The following protocol produces a supernatant containing polypeptide of the present invention to be tested. This supernatant can then be used in the Screening Assays described in Examples 33-42.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working  
20 solution of 50ug/ml. Add 200  $\mu$ l of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for  
25 up to two weeks.

Plate 293T cells (do not carry cells past P+20) at  $2 \times 10^5$  cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

30 The next day, mix together in a sterile solution basin: 300  $\mu$ l Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing

a polynucleotide insert, produced by the methods described in Examples 8-10, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add  
5 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then  
10 person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a 12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37 degree C for 6 hours.

While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with  
15 1x penstrep, or HGS CHO-5 media (116.6 mg/L of CaCl<sub>2</sub> (anhyd); 0.00130 mg/L CuSO<sub>4</sub>-5H<sub>2</sub>O; 0.050 mg/L of Fe(NO<sub>3</sub>)<sub>3</sub>-9H<sub>2</sub>O; 0.417 mg/L of FeSO<sub>4</sub>-7H<sub>2</sub>O; 311.80 mg/L of KCl; 28.64 mg/L of MgCl<sub>2</sub>; 48.84 mg/L of MgSO<sub>4</sub>; 6995.50 mg/L of NaCl; 2400.0 mg/L of NaHCO<sub>3</sub>; 62.50 mg/L of NaH<sub>2</sub>PO<sub>4</sub>-H<sub>2</sub>O; 71.02 mg/L of Na<sub>2</sub>HPO<sub>4</sub>; .4320 mg/L of ZnSO<sub>4</sub>-7H<sub>2</sub>O; .002 mg/L of Arachidonic Acid ; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-  
20 Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L- Arginine-HCL; 7.50 mg/ml of L-Asparagine-H<sub>2</sub>O; 6.65 mg/ml of L-Aspartic Acid; 29.56  
25 mg/ml of L-Cystine-2HCL-H<sub>2</sub>O; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L- Glutamic Acid; 365.0 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L- Histidine-HCL-H<sub>2</sub>O; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalanine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22  
30 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tyrosine-2Na-2H<sub>2</sub>O; and 99.65 mg/ml of L-

Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; 0.680 mg/L of Vitamin B<sub>12</sub>; 25 mM of  
5 HEPES Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal Acetate. Adjust  
10 osmolarity to 327 mOsm) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml  
15 appropriate media to each well. Incubate at 37 degree C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 33-40.

20 It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide of the present invention directly (e.g., as a secreted protein) or by polypeptide of the present invention inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant  
25 characterized by an activity in a particular assay.

#### *Example 32: Construction of GAS Reporter Construct*

One signal transduction pathway involved in the differentiation and proliferation of  
30 cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements

alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has  
5 been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon  
10 tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below.  
15 (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved  
20 cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:838)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

25 Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

381

	<u>Ligand</u>	<u>JAKs</u>				<u>STATS GAS(elements) or ISRE</u>	
		<u>tyk2</u>	<u>Jak1</u>	<u>Jak2</u>	<u>Jak3</u>		
	<u>IFN family</u>						
5	IFN-a/B	+	+	-	-	1,2,3	ISRE
	IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
	IL-10	+	?	?	-	1,3	
	<u>gp130 family</u>						
10	IL-6 (Pleiotrohic)	+	+	+	?	1,3	GAS (IRF1>Lys6>IFP)
	IL-11(Pleiotrohic)	?	+	?	?	1,3	
	OnM(Pleiotrohic)	?	+	+	?	1,3	
	LIF(Pleiotrohic)	?	+	+	?	1,3	
	CNTF(Pleiotrohic)	-/+	+	+	?	1,3	
15	G-CSF(Pleiotrohic)	?	+	?	?	1,3	
	IL-12(Pleiotrohic)	+	-	+	+	1,3	
	<u>g-C family</u>						
	IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
20	IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP
	>>Ly6)(IgH)						
	IL-7 (lymphocytes)	-	+	-	+	5	GAS
	IL-9 (lymphocytes)	-	+	-	+	5	GAS
	IL-13 (lymphocyte)	-	+	?	?	6	GAS
25	IL-15	?	+	?	+	5	GAS
	<u>gp140 family</u>						
	IL-3 (myeloid)	-	-	+	-	5	GAS (IRF1>IFP>>Ly6)
	IL-5 (myeloid)	-	-	+	-	5	GAS
30	GM-CSF (myeloid)	-	-	+	-	5	GAS
	<u>Growth hormone family</u>						
	GH	?	-	+	-	5	
	PRL	?	+/-	+	-	1,3,5	
35	EPO	?	-	+	-	5	GAS(B-

382

CAS&gt;IRF1=IFP&gt;&gt;Ly6)

Receptor Tyrosine Kinases

	EGF	?	+	+	-	1,3	GAS (IRF1)
5	PDGF	?	+	+	-	1,3	
	CSF-1	?	+	+	-	1,3	GAS (not IRF1)

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 33-34, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

10 5':GCGCCTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCGAAATGATTTCCTCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:839)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTGGCAAAGCCTAGGC:3' (SEQ ID NO:840)

15 PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

20 5':CTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCGAAATGATTTCCTCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCGCCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTA  
25 GGCTTTTGGAAAAAGCTT:3' (SEQ ID NO:841)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol

30

acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 33-34.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 35 and 36. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

*Example 33: High-Throughput Screening Assay for T-cell Activity.*

The following protocol is used to assess T-cell activity by identifying factors, and determining whether supernate containing a polypeptide of the invention proliferates and/or differentiates T-cells. T-cell activity is assessed using the



GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC  
5 Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4<sup>+</sup> Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately  
10 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells  
15 containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies) with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

20 During the incubation period, count cell concentration, spin down the required number of cells ( $10^7$  per transfection), and resuspend in OPTI-MEM to a final concentration of  $10^7$  cells/ml. Then add 1ml of  $1 \times 10^7$  cells in OPTI-MEM to T25 flask and incubate at 37 degree C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

25 The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Gentamicin, and 1% Pen-Strep. These cells are treated with supernatants containing polypeptide of the present invention or polypeptide of the present invention induced polypeptides as produced by the protocol described in Example 31.

30 On the day of treatment with the supernatant, the cells should be washed and

resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

- 5           Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

- After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12  
10   channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

- The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul  
15   samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20 degree C until SEAP assays are performed according to Example 37. The plates containing the remaining treated cells are placed at 4 degree C and serve as a source of material for repeating the assay on a specific well if desired.

- 20           As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

- The above protocol may be used in the generation of both transient, as well as, stable transfected cells, which would be apparent to those of skill in the art.

25

*Example 34: High-Throughput Screening Assay Identifying Myeloid Activity*

- The following protocol is used to assess myeloid activity of polypeptide of the present invention by determining whether polypeptide of the present invention  
30   proliferates and/or differentiates myeloid cells. Myeloid cell activity is assessed using

the GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

5 To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 32, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest  $2 \times 10^7$  U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml  
10 penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM  $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ , 1 mM  $\text{MgCl}_2$ , and 675 uM  $\text{CaCl}_2$ . Incubate at 37 degrees C for 45 min.

15 Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37 degree C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

20 These cells are tested by harvesting  $1 \times 10^8$  cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of  $5 \times 10^5$  cells/ml. Plate 200 ul cells per well in the 96-well plate (or  $1 \times 10^5$  cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example  
25 31. Incubate at 37 degree C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 37.

30 *Example 35: High-Throughput Screening Assay Identifying Neuronal Activity.*

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed by polypeptide of the present invention.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat pheochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells by polypeptide of the present invention can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:842)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:843)

Using the GAS:SEAP/Neo vector produced in Example 32, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and

allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and  
5 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 31. EGR-SEAP/PC12 stable cells are obtained by  
10 growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS  
15 (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as  $5 \times 10^5$   
20 cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to  $1 \times 10^5$  cells/well). Add 50 ul supernatant produced by Example 31, 37 degree C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over  
25 fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 37.

*Example 36: High-Throughput Screening Assay for T-cell Activity*

30 NF-KB (Nuclear Factor KB) is a transcription factor activated by a wide

variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-KB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- KB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- KB is retained in the cytoplasm with I-KB (Inhibitor KB). However, upon stimulation, I- KB is phosphorylated and degraded, causing NF- KB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- KB include IL-2, IL-6, GM-CSF, ICAM-1 and class I MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-KB promoter element are used to screen the supernatants produced in Example 31. Activators or inhibitors of NF-KB would be useful in treating, preventing, and/or diagnosing diseases. For example, inhibitors of NF-KB could be used to treat those diseases related to the acute or chronic activation of NF-KB, such as rheumatoid arthritis.

To construct a vector containing the NF-KB promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF-KB binding site (GGGGACTTTCCC) (SEQ ID NO:844), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC  
TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:845)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTGGCAAAGCCTAGGC:3' (SEQ ID NO:840)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene)

Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCC  
ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCC  
5 ATCCCGCCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCGATGGCTGA  
CTAATTTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTA  
TTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAA  
GCTT:3' (SEQ ID NO:846)

Next, replace the SV40 minimal promoter element present in the pSEAP2-  
10 promoter plasmid (Clontech) with this NF-KB/SV40 fragment using XhoI and  
HindIII. However, this vector does not contain a neomycin resistance gene, and  
therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF-KB/SV40/SEAP  
cassette is removed from the above NF-KB/SEAP vector using restriction enzymes  
15 SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly,  
the NF-KB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the  
GFP gene, after restricting pGFP-1 with SalI and NotI.

Once NF-KB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are  
created and maintained according to the protocol described in Example 33. Similarly,  
20 the method for assaying supernatants with these stable Jurkat T-cells is also described  
in Example 33. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to  
wells H9, H10, and H11, with a 5-10 fold activation typically observed.

#### *Example 37: Assay for SEAP Activity*

25

As a reporter molecule for the assays described in Examples 33-36, SEAP  
activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the  
following general procedure. The Tropix Phospho-light Kit supplies the Dilution,  
Assay, and Reaction Buffers used below.

30

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 ul of 2.5x

dilution buffer into Optiplates containing 35 ul of a supernatant. Seal the plates with a plastic sealer and incubate at 65 degree C for 30 min. Separate the Optiplates to avoid uneven heating.

- 5 Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 ml Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 ul Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at
- 10 each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

#### Reaction Buffer Formulation:

15

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6
23	125	6.25



393

24	130	6.5
25	135	6.75
26	140	7
27	145	7.25
28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

---

*Example 38: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability*

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants  
5 which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to  
10 measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-4 (Molecular Probes, Inc.; catalog no. F-14202), used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star  
15 black 96-well plate with clear bottom. The plate is incubated in a CO<sub>2</sub> incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-4 is made in 10% pluronic acid DMSO. To load the cells with fluo-4, 50 ul of 12 ug/ml fluo-4 is added to each well. The plate  
20 is incubated at 37 degrees C in a CO<sub>2</sub> incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to  $2-5 \times 10^6$  cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-4 solution in 10% pluronic acid DMSO is added to each ml of cell suspension.  
25 The tube is then placed in a 37 degrees C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to  $1 \times 10^6$  cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley Cell Wash with 200 ul, followed by an aspiration step to 100 ul final volume.

30 For a non-cell based assay, each well contains a fluorescent molecule, such as

fluo-4 . The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event caused by the a molecule, either polypeptide of the present invention or a molecule induced by polypeptide of the present invention, which has resulted in an increase in the intracellular  $\text{Ca}^{++}$  concentration.

10

*Example 40: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity*

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

20       Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

25       Because of the wide range of known factors capable of stimulating tyrosine kinase activity, identifying whether polypeptide of the present invention or a molecule induced by polypeptide of the present invention is capable of activating tyrosine kinase signal transduction pathways is of interest. Therefore, the following protocol

30

is designed to identify such molecules capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed with PBS and stored at 4 degree C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 31, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na<sub>3</sub>VO<sub>4</sub>, 2 mM Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub> and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4

degree C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

5        Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for  
10 a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg<sub>2</sub><sup>+</sup> (5mM ATP/50mM MgCl<sub>2</sub>), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl<sub>2</sub>, 5 mM MnCl<sub>2</sub>,  
15 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30 degree C for 2 min. Initiate the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA and place the reactions on ice.

20        Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37 degree C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-  
25 POD(0.5u/ml)) to each well and incubate at 37 degree C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound  
30 peroxidase activity is quantitated using an ELISA reader and reflects the level of

tyrosine kinase activity.

*Example 41: High-Throughput Screening Assay Identifying Phosphorylation Activity*

5           As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 40, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other  
10       molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

          Specifically, assay plates are made by coating the wells of a 96-well ELISA  
15       plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody  
20       detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4 degree C until use.

          A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants  
25       obtained in Example 31 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

          After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit)  
30       antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the

Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased  
5 fluorescent signal over background indicates a phosphorylation by polypeptide of the present invention or a molecule induced by polypeptide of the present invention.

*Example 42: Assay for the Stimulation of Bone Marrow CD34+ Cell Proliferation*

10 This assay is based on the ability of human CD34+ to proliferate in the presence of hematopoietic growth factors and evaluates the ability of isolated polypeptides expressed in mammalian cells to stimulate proliferation of CD34+ cells.

It has been previously shown that most mature precursors will respond to only a single signal. More immature precursors require at least two signals to respond.  
15 Therefore, to test the effect of polypeptides on hematopoietic activity of a wide range of progenitor cells, the assay contains a given polypeptide in the presence or absence of other hematopoietic growth factors. Isolated cells are cultured for 5 days in the presence of Stem Cell Factor (SCF) in combination with tested sample. SCF alone has a very limited effect on the proliferation of bone marrow (BM) cells, acting in  
20 such conditions only as a "survival" factor. However, combined with any factor exhibiting stimulatory effect on these cells (e.g., IL-3), SCF will cause a synergistic effect. Therefore, if the tested polypeptide has a stimulatory effect on a hematopoietic progenitors, such activity can be easily detected. Since normal BM cells have a low level of cycling cells, it is likely that any inhibitory effect of a given polypeptide, or  
25 agonists or antagonists thereof, might not be detected. Accordingly, assays for an inhibitory effect on progenitors is preferably tested in cells that are first subjected to *in vitro* stimulation with SCF+IL+3, and then contacted with the compound that is being evaluated for inhibition of such induced proliferation.

Briefly, CD34+ cells are isolated using methods known in the art. The cells  
30 are thawed and resuspended in medium (QBSF 60 serum-free medium with 1% L-

glutamine (500ml) Quality Biological, Inc., Gaithersburg, MD Cat# 160-204-101). After several gentle centrifugation steps at 200 x g, cells are allowed to rest for one hour. The cell count is adjusted to  $2.5 \times 10^5$  cells/ml. During this time, 100  $\mu$ l of sterile water is added to the peripheral wells of a 96-well plate. The cytokines that  
5 can be tested with a given polypeptide in this assay is rhSCF (R&D Systems, Minneapolis, MN, Cat# 255-SC) at 50 ng/ml alone and in combination with rhSCF and rhIL-3 (R&D Systems, Minneapolis, MN, Cat# 203-ML) at 30 ng/ml. After one hour, 10  $\mu$ l of prepared cytokines, 50  $\mu$ l of the supernatants prepared in Example 31 (supernatants at 1:2 dilution = 50  $\mu$ l) and 20  $\mu$ l of diluted cells are added to the media  
10 which is already present in the wells to allow for a final total volume of 100  $\mu$ l. The plates are then placed in a 37°C/5% CO<sub>2</sub> incubator for five days.

Eighteen hours before the assay is harvested, 0.5  $\mu$ Ci/well of [3H] Thymidine is added in a 10  $\mu$ l volume to each well to determine the proliferation rate. The experiment is terminated by harvesting the cells from each 96-well plate to a filtermat  
15 using the Tomtec Harvester 96. After harvesting, the filtermats are dried, trimmed and placed into OmniFilter assemblies consisting of one OmniFilter plate and one OmniFilter Tray. 60  $\mu$ l Microscint is added to each well and the plate sealed with TopSeal-A press-on sealing film. A bar code 15 sticker is affixed to the first plate for counting. The sealed plates is then loaded and the level of radioactivity determined  
20 via the Packard Top Count and the printed data collected for analysis. The level of radioactivity reflects the amount of cell proliferation.

The studies described in this example test the activity of a given polypeptide to stimulate bone marrow CD34+ cell proliferation. One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene  
25 therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof. As a nonlimiting example, potential antagonists tested in this assay would be expected to inhibit cell proliferation in the presence of cytokines and/or to increase the inhibition of cell proliferation in the presence of cytokines and a given polypeptide. In contrast, potential agonists tested in this assay would be expected to enhance cell  
30 proliferation and/or to decrease the inhibition of cell proliferation in the presence of



cytokines and a given polypeptide.

The ability of a gene to stimulate the proliferation of bone marrow CD34+ cells indicates that polynucleotides and polypeptides corresponding to the gene are useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and  
5 "Infectious Disease" sections above, and elsewhere herein.

*Example 43: Assay for Extracellular Matrix Enhanced Cell Response (EMECR)*

10 The objective of the Extracellular Matrix Enhanced Cell Response (EMECR) assay is to identify gene products (e.g., isolated polypeptides) that act on the hematopoietic stem cells in the context of the extracellular matrix (ECM) induced signal.

Cells respond to the regulatory factors in the context of signal(s) received from  
15 the surrounding microenvironment. For example, fibroblasts, and endothelial and epithelial stem cells fail to replicate in the absence of signals from the ECM. Hematopoietic stem cells can undergo self-renewal in the bone marrow, but not in *in vitro* suspension culture. The ability of stem cells to undergo self-renewal *in vitro* is dependent upon their interaction with the stromal cells and the ECM protein  
20 fibronectin (fn). Adhesion of cells to fn is mediated by the  $\alpha_5\beta_1$  and  $\alpha_4\beta_1$  integrin receptors, which are expressed by human and mouse hematopoietic stem cells. The factor(s) which integrate with the ECM environment and responsible for stimulating stem cell self-renewal has not yet been identified. Discovery of such factors should be of great interest in gene therapy and bone marrow transplant applications

25 Briefly, polystyrene, non tissue culture treated, 96-well plates are coated with fn fragment at a coating concentration of  $0.2 \mu\text{g}/\text{cm}^2$ . Mouse bone marrow cells are plated (1,000 cells/well ) in 0.2 ml of serum-free medium. Cells cultured in the presence of IL-3 ( 5 ng/ml ) + SCF ( 50 ng/ml ) would serve as the positive control, conditions under which little self-renewal but pronounced differentiation of the stem

cells is to be expected. Gene products of the invention (e.g., including, but not limited to, polynucleotides and polypeptides of the present invention, and supernatants produced in Example 31), are tested with appropriate negative controls in the presence and absence of SCF(5.0 ng/ml), where test factor supernates represent 10% of the total assay volume. The plated cells are then allowed to grow by incubating in a low oxygen environment ( 5% CO<sub>2</sub>, 7% O<sub>2</sub>, and 88% N<sub>2</sub> ) tissue culture incubator for 7 days. The number of proliferating cells within the wells is then quantitated by measuring thymidine incorporation into cellular DNA. Verification of the positive hits in the assay will require phenotypic characterization of the cells, which can be accomplished by scaling up of the culture system and using appropriate antibody reagents against cell surface antigens and FACScan.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

If a particular polypeptide of the present invention is found to be a stimulator of hematopoietic progenitors, polynucleotides and polypeptides corresponding to the gene encoding said polypeptide may be useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein. The gene product may also be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Additionally, the polynucleotides and/or polypeptides of the gene of interest and/or agonists and/or antagonists thereof, may also be employed to inhibit the proliferation and differentiation of hematopoietic cells and therefore may be employed to protect bone marrow stem cells from chemotherapeutic agents during chemotherapy. This antiproliferative effect may allow administration of higher doses of chemotherapeutic agents and, therefore, more effective chemotherapeutic treatment.

Moreover, polynucleotides and polypeptides corresponding to the gene of

interest may also be useful for the treatment and diagnosis of hematopoietic related disorders such as, for example, anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex-vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia.

*Example 44: Human Dermal Fibroblast and Aortic Smooth Muscle Cell Proliferation*

10       The polypeptide of interest is added to cultures of normal human dermal fibroblasts (NHDF) and human aortic smooth muscle cells (AoSMC) and two co-assays are performed with each sample. The first assay examines the effect of the polypeptide of interest on the proliferation of normal human dermal fibroblasts (NHDF) or aortic smooth muscle cells (AoSMC). Aberrant growth of fibroblasts or  
15       smooth muscle cells is a part of several pathological processes, including fibrosis, and restenosis. The second assay examines IL6 production by both NHDF and SMC. IL6 production is an indication of functional activation. Activated cells will have increased production of a number of cytokines and other factors, which can result in a proinflammatory or immunomodulatory outcome. Assays are run with and without  
20       co-TNF $\alpha$  stimulation, in order to check for costimulatory or inhibitory activity.

Briefly, on day 1, 96-well black plates are set up with 1000 cells/well (NHDF) or 2000 cells/well (AoSMC) in 100  $\mu$ l culture media. NHDF culture media contains: Clonetics FB basal media, 1mg/ml hFGF, 5mg/ml insulin, 50mg/ml gentamycin, 2%FBS, while AoSMC culture media contains Clonetics SM basal media, 0.5  $\mu$ g/ml  
25       hEGF, 5mg/ml insulin, 1 $\mu$ g/ml hFGF, 50mg/ml gentamycin, 50  $\mu$ g/ml Amphotericin B, 5%FBS. After incubation at 37°C for at least 4-5 hours, culture media is aspirated and replaced with growth arrest media. Growth arrest media for NHDF contains fibroblast basal media, 50mg/ml gentamycin, 2% FBS, while growth arrest media for AoSMC contains SM basal media, 50mg/ml gentamycin, 50 $\mu$ g/ml Amphotericin B,  
30       0.4% FBS. Incubate at 37°C until day 2.

On day 2, serial dilutions and templates of the polypeptide of interest are designed such that they always include media controls and known-protein controls. For both stimulation and inhibition experiments, proteins are diluted in growth arrest media. For inhibition experiments, TNF $\alpha$  is added to a final concentration of 2ng/ml (NHDF) or 5ng/ml (AoSMC). Add 1/3 vol media containing controls or polypeptides  
5 of the present invention and incubate at 37°C/5% CO<sub>2</sub> until day 5.

Transfer 60 $\mu$ l from each well to another labeled 96-well plate, cover with a plate-sealer, and store at 4°C until Day 6 (for IL6 ELISA). To the remaining 100  $\mu$ l in the cell culture plate, aseptically add Alamar Blue in an amount equal to 10% of the  
10 culture volume (10 $\mu$ l). Return plates to incubator for 3 to 4 hours. Then measure fluorescence with excitation at 530nm and emission at 590nm using the CytoFluor. This yields the growth stimulation/inhibition data.

On day 5, the IL6 ELISA is performed by coating a 96 well plate with 50-100  $\mu$ l/well of Anti-Human IL6 Monoclonal antibody diluted in PBS, pH 7.4, incubate ON  
15 at room temperature.

On day 6, empty the plates into the sink and blot on paper towels. Prepare Assay Buffer containing PBS with 4% BSA. Block the plates with 200  $\mu$ l/well of Pierce Super Block blocking buffer in PBS for 1-2 hr and then wash plates with wash buffer (PBS, 0.05% Tween-20). Blot plates on paper towels. Then add 50  $\mu$ l/well of  
20 diluted Anti-Human IL-6 Monoclonal, Biotin-labeled antibody at 0.50 mg/ml. Make dilutions of IL-6 stock in media (30, 10, 3, 1, 0.3, 0 ng/ml). Add duplicate samples to top row of plate. Cover the plates and incubate for 2 hours at RT on shaker. Plates are washed with wash buffer and blotted on paper towels. Dilute EU-labeled Streptavidin 1:1000 in Assay buffer, and add 100  $\mu$ l/well. Cover the plate and incubate 1 h at RT.  
25 Plates are again washed with wash buffer and blotted on paper towels. Add 100  $\mu$ l/well of Enhancement Solution and shake for 5 minutes. Read the plate on the Wallac DELFIA Fluorometer. Readings from triplicate samples in each assay are tabulated and averaged.

A positive result in this assay suggests AoSMC cell proliferation and that the  
30 polypeptide of the present invention may be involved in dermal fibroblast

proliferation and/or smooth muscle cell proliferation. A positive result also suggests many potential uses of polypeptides, polynucleotides, agonists and/or antagonists of the polynucleotide/polypeptide of the present invention which gives a positive result. For example, inflammation and immune responses, wound healing, and angiogenesis, as detailed throughout this specification. Particularly, polypeptides of the present invention and polynucleotides of the present invention may be used in wound healing and dermal regeneration, as well as the promotion of vasculargenesis, both of the blood vessels and lymphatics. The growth of vessels can be used in the treatment of, for example, cardiovascular diseases. Additionally, antagonists of polypeptides and polynucleotides of the invention may be useful in treating diseases, disorders, and/or conditions which involve angiogenesis by acting as an anti-vascular (e.g., anti-angiogenesis). These diseases, disorders, and/or conditions are known in the art and/or are described herein, such as, for example, malignancies, solid tumors, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophilic joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis. Moreover, antagonists of polypeptides and polynucleotides of the invention may be useful in treating anti-hyperproliferative diseases and/or anti-inflammatory known in the art and/or described herein.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

*Example 45: Cellular Adhesion Molecule (CAM) Expression on Endothelial Cells*

5           The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1  
10 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor  
15 participate in the modulation of the expression of these CAMs.

Briefly, endothelial cells (e.g., Human Umbilical Vein Endothelial cells (HUVECs)) are grown in a standard 96 well plate to confluence, growth medium is removed from the cells and replaced with 100  $\mu$ l of 199 Medium (10% fetal bovine serum (FBS)). Samples for testing and positive or negative controls are added to the  
20 plate in triplicate (in 10  $\mu$ l volumes). Plates are then incubated at 37°C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100  $\mu$ l of 0.1% paraformaldehyde-PBS(with Ca++ and Mg++) is added to each well. Plates are held at 4°C for 30 min. Fixative is removed from the wells and wells are washed 1X with PBS(+Ca,Mg) + 0.5% BSA  
25 and drained. 10  $\mu$ l of diluted primary antibody is added to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10  $\mu$ g/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed three times with PBS(+Ca,Mg) + 0.5% BSA. 20  $\mu$ l of diluted ExtrAvidin-Alkaline  
30 Phosphotase (1:5,000 dilution, referred to herein as the working dilution) are added to

each well and incubated at 37°C for 30 min. Wells are washed three times with PBS(+Ca,Mg)+0.5% BSA. Dissolve 1 tablet of p-Nitrophenol Phosphate pNPP per 5 ml of glycine buffer (pH 10.4). 100 µl of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphatase in glycine buffer: 1:5,000 ( $10^0$ ) >  $10^{-0.5}$  >  $10^{-1}$  >  $10^{-1.5}$ . 5 µl of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 µl of pNPP reagent is then added to each of the standard wells. The plate is incubated at 37°C for 4h. A volume of 50 µl of 3M NaOH is added to all wells. The plate is read on a plate reader at 405 nm using the background subtraction option on blank wells filled with glycine buffer only. Additionally, the template is set up to indicate the concentration of AP-conjugate in each standard well [ 5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

15 *Example 46: Alamar Blue Endothelial Cells Proliferation Assay*

This assay may be used to quantitatively determine protein mediated inhibition of bFGF-induced proliferation of Bovine Lymphatic Endothelial Cells (LECs), Bovine Aortic Endothelial Cells (BAECs) or Human Microvascular Uterine Myometrial Cells (UTMECs). This assay incorporates a fluorometric growth indicator based on detection of metabolic activity. A standard Alamar Blue Proliferation Assay is prepared in EGM-2MV with 10 ng /ml of bFGF added as a source of endothelial cell stimulation. This assay may be used with a variety of endothelial cells with slight changes in growth medium and cell concentration. Dilutions of the protein batches to be tested are diluted as appropriate. Serum-free medium (GIBCO SFM) without bFGF is used as a non-stimulated control and Angiostatin or TSP-1 are included as a known inhibitory controls.

Briefly, LEC, BAECs or UTMECs are seeded in growth media at a density of 5000 to 2000 cells/well in a 96 well plate and placed at 37-C overnight. After the overnight incubation of the cells, the growth media is removed and replaced with

GIBCO EC-SFM. The cells are treated with the appropriate dilutions of the protein of interest or control protein sample(s) (prepared in SFM ) in triplicate wells with additional bFGF to a concentration of 10 ng/ ml. Once the cells have been treated with the samples, the plate(s) is/are placed back in the 37° C incubator for three days.

- 5 After three days 10 ml of stock alamar blue (Biosource Cat# DAL1100) is added to each well and the plate(s) is/are placed back in the 37°C incubator for four hours. The plate(s) are then read at 530nm excitation and 590nm emission using the CytoFluor fluorescence reader. Direct output is recorded in relative fluorescence units.

- Alamar blue is an oxidation-reduction indicator that both fluoresces and  
10 changes color in response to chemical reduction of growth medium resulting from cell growth. As cells grow in culture, innate metabolic activity results in a chemical reduction of the immediate surrounding environment. Reduction related to growth causes the indicator to change from oxidized (non-fluorescent blue) form to reduced (fluorescent red) form. i.e. stimulated proliferation will produce a stronger signal and  
15 inhibited proliferation will produce a weaker signal and the total signal is proportional to the total number of cells as well as their metabolic activity. The background level of activity is observed with the starvation medium alone. This is compared to the output observed from the positive control samples (bFGF in growth medium) and protein dilutions.

20

*Example 47: Detection of Inhibition of a Mixed Lymphocyte Reaction*

This assay can be used to detect and evaluate inhibition of a Mixed Lymphocyte Reaction (MLR) by gene products (e.g., isolated polypeptides).

- 25 Inhibition of a MLR may be due to a direct effect on cell proliferation and viability, modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, or modulation of cytokine production by accessory cells. Multiple cells may be targeted by these polypeptides since the peripheral blood mononuclear fraction used in this assay includes T, B and



natural killer lymphocytes, as well as monocytes and dendritic cells.

Polypeptides of interest found to inhibit the MLR may find application in diseases associated with lymphocyte and monocyte activation or proliferation. These include, but are not limited to, diseases such as asthma, arthritis, diabetes, inflammatory skin conditions, psoriasis, eczema, systemic lupus erythematosus, multiple sclerosis, glomerulonephritis, inflammatory bowel disease, crohn's disease, ulcerative colitis, arteriosclerosis, cirrhosis, graft vs. host disease, host vs. graft disease, hepatitis, leukemia and lymphoma.

Briefly, PBMCs from human donors are purified by density gradient centrifugation using Lymphocyte Separation Medium (LSM<sup>®</sup>, density 1.0770 g/ml, Organon Teknika Corporation, West Chester, PA). PBMCs from two donors are adjusted to  $2 \times 10^6$  cells/ml in RPMI-1640 (Life Technologies, Grand Island, NY) supplemented with 10% FCS and 2 mM glutamine. PBMCs from a third donor is adjusted to  $2 \times 10^5$  cells/ml. Fifty microliters of PBMCs from each donor is added to wells of a 96-well round bottom microtiter plate. Dilutions of test materials (50  $\mu$ l) is added in triplicate to microtiter wells. Test samples (of the protein of interest) are added for final dilution of 1:4; rhuIL-2 (R&D Systems, Minneapolis, MN, catalog number 202-IL) is added to a final concentration of 1  $\mu$ g/ml; anti-CD4 mAb (R&D Systems, clone 34930.11, catalog number MAB379) is added to a final concentration of 10  $\mu$ g/ml. Cells are cultured for 7-8 days at 37°C in 5% CO<sub>2</sub>, and 1  $\mu$ C of [<sup>3</sup>H] thymidine is added to wells for the last 16 hrs of culture. Cells are harvested and thymidine incorporation determined using a Packard TopCount. Data is expressed as the mean and standard deviation of triplicate determinations.

Samples of the protein of interest are screened in separate experiments and compared to the negative control treatment, anti-CD4 mAb, which inhibits proliferation of lymphocytes and the positive control treatment, IL-2 (either as recombinant material or supernatant), which enhances proliferation of lymphocytes.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

- 5           The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both
- 10 incorporated herein by reference in their entirety. Moreover, the hard copy of and the corresponding computer readable form of the Sequence Listing of Serial No. 60/124,270 are also incorporated herein by reference in their entirety.

Applicant's or agent's file reference number	411 PA103PCT	International application no.
---	-----------------	-------------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>10801 University Boulevard</u> <u>Manassas, Virginia 20110-2209</u> <u>United States of America</u>	
Date of deposit <u>20 May 1997</u>	Accession Number <u>209059</u>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US 08 MAR 2000</b>	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer <u>Torilisa Harrod</u> <u>PCT/Internat'l Appl Processing Div.</u> <u>(703) 305-3670</u>	Authorized officer 

**ATCC Deposit No. 209059****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209059

#### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

414

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <b>American Type Culture Collection</b>	
Address of depositary institution (including postal code and country) <b>10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</b>	
Date of deposit <b>20 May 1997</b>	Accession Number <b>209060</b>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only <input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US 08 MAR 2000</b> Authorized officer <b>Yolanda Harrod</b> <b>PCT/Internat'l Appl Processing Div.</b> <b>(703) 305-3670</b>	For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
---	---

**ATCC Deposit No. 209060****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209060

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.



417

Applicant's or agent's file reference number	PA103PCT	International application N
---	----------	-----------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>10801 University Boulevard</u> <u>Manassas, Virginia 20110-2209</u> <u>United States of America</u>	
Date of deposit <u>20 May 1997</u>	Accession Number <u>209061</u>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<input checked="" type="checkbox"/> For receiving Office use only
<input checked="" type="checkbox"/> This sheet was received with the international application
<b>RO/US</b> <b>03 MAR 2000</b>
Authorized officer <u>Toranda Harrod</u> <u>PCT/Internat'l Appl Processing Div.</u> <u>(703) 305-3870</u>

<input type="checkbox"/> For International Bureau use only
<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer

**ATCC Deposit No. 209061****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**

**ATCC Deposit No. 209061**

## **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

420

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution  American Type Culture Collection	
Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit  20 May 1997	Accession Number  209062
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")          	

<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US 03 MAR 2000</b> Authorized officer <b>Yolanda Harrod</b> <b>PCT/Internat'l Appl Processing Div.</b> <b>(703) 305-3570</b>	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on:  Authorized officer
--	--

**ATCC Deposit No. 209062****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**

**ATCC Deposit No. 209062**

## **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

423

Applicant's or agent's file reference number	PA103PCT	International application i
---	----------	-----------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT <span style="float: right;">Further deposits are identified on an additional sheet <input type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>10801 University Boulevard</u> <u>Manassas, Virginia 20110-2209</u> <u>United States of America</u>	
Date of deposit <u>20 May 1997</u>	Accession Number <u>209063</u>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<p>For receiving Office use only</p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <p><b>RO/US 20 MAR 2000</b></p> <p>Authorized officer <u>Yolanda Harrod</u> <u>PCT/Internat'l Appl Processing Div.</u> <u>(703) 305-9670</u></p>	<p>For International Bureau use only</p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
---	--

**ATCC Deposit No. 209063****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection. the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.



Page 2

ATCC Deposit No. 209063

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

426

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>10801 University Boulevard</u> <u>Manassas, Virginia 20110-2209</u> <u>United States of America</u>	
Date of deposit <u>20 May 1997</u>	Accession Number <u>209064</u>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only <input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US 09 MAR 2000</b> Authorized officer <b>Yolanda Harrod</b> <b>PCT/Internat'l Appl Processing Div.</b> <b>(703) 305-3670</b>	For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
---	---

**ATCC Deposit No. 209064****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2  
ATCC Deposit No. 209064

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

429

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>10801 University Boulevard</u> <u>Manassas, Virginia 20110-2709</u> <u>United States of America</u>	
Date of deposit <u>20 May 1997</u>	Accession Number <u>209065</u>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<input checked="" type="checkbox"/> For receiving Office use only This sheet was received with the international application <b>RO/US 09 MAR 2000</b> Authorized officer: <u>Isabella Harco</u> <u>PCT/Int'l Appl Processing Div.</u> <u>(703) 305-3370</u>	<input type="checkbox"/> For International Bureau use only This sheet was received by the International Bureau on: Authorized officer: _____
--	--

**ATCC Deposit No. 209065****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209065

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

432

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution  American Type Culture Collection	
Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit  20 May 1997	Accession Number  209066
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
<b>RO/US</b> <b>06 MAR 2000</b> Authorized officer: Yolande Harrod PCT/Int'l Appl Processing Div. (703) 305-3670	Authorized officer



**ATCC Deposit No. 209066****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2  
ATCC Deposit No. 209066

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

435

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <p style="text-align: center;">American Type Culture Collection</p>	
Address of depositary institution (including postal code and country) <p style="text-align: center;">10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</p>	
Date of deposit <p style="text-align: center;">20 May 1997</p>	Accession Number <p style="text-align: center;">209067</p>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US</b> <b>J3 MAR 2000</b> Authorized officer <b>Yolanda Harrod</b> <b>PCT/Internat'l Appl Processing Div.</b> <b>(700) 385-3670</b>	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
---	--

**ATCC Deposit No. 209067****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**

**ATCC Deposit No. 209067**

## **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

438

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <b>American Type Culture Collection</b>	
Address of depositary institution (including postal code and country) <b>10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</b>	
Date of deposit <b>20 May 1997</b>	Accession Number <b>209068</b>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only
<input checked="" type="checkbox"/> This sheet was received with the international application
<b>RO/US 03 MAR 2000</b>
Authorized officer <b>Yolanda Harrod</b> <b>PCT/Internat'l Appl Processing Div.</b> <b>(703) 305-3870</b>

For International Bureau use only
<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer

**ATCC Deposit No. 209068****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**

**ATCC Deposit No. 209068**

## **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.



441

Applicant's or agent's file reference number	PA103PCT	International application
--	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <b>American Type Culture Collection</b>	
Address of depositary institution (including postal code and country)  <b>10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</b>	
Date of deposit <b>20 May 1997</b>	Accession Number <b>209069</b>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US 05 MAR 2000</b> Authorized officer <b>Patricia Harrod</b> <b>PCT/Int'l App. Processing Div.</b> <b>(703) 305-3879</b>	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
--	--

**ATCC Deposit No. 209069****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2  
ATCC Deposit No. 209069

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

444

Applicant's or agent's file reference number	PA103PCT	International application
--	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 12 January 1998	Accession Number 209579
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application RECEIVED 02 MAR 2000	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer [Signature]	Authorized officer [Signature]

**ATCC Deposit No. 209579****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**

**ATCC Deposit No. 209579**

## **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

447

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution  American Type Culture Collection	
Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit  12 January 1998	Accession Number  209578
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
<b>RO/US 03 MAR 2000</b>	
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (800) 365-3670	Authorized officer

**ATCC Deposit No. 209578****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.



Page 2

ATCC Deposit No. 209578

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

450

Applicant's or agent's file reference number	PA103PCT	International application
--	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 16 July 1998	Accession Number 203067
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer RO/US 08 MAR 2000 PCT/Intemat'l Appl Processing Div 703A 305-3670	Authorized officer

**ATCC Deposit No. 203067****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 203067

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

453

Applicant's or agent's file reference number	PA103PCT	International application
---	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <p style="text-align: center;">American Type Culture Collection</p>	
Address of depositary institution (including postal code and country) <p style="text-align: center;">10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</p>	
Date of deposit <p style="text-align: center;">16 July 1998</p>	Accession Number <p style="text-align: center;">203068</p>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<input checked="" type="checkbox"/> For receiving Office use only This sheet was received with the international application <b>RO/US 03 MAR 2000</b> Authorized officer <b>Yolanda Harrod</b> PCT/Internat'l Appl Processing Div. <b>7031 305 3020</b>	<input type="checkbox"/> For International Bureau use only This sheet was received by the International Bureau on: Authorized officer
---	---

**ATCC Deposit No. 203068****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2  
ATCC Deposit No. 203068

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

456

Applicant's or agent's file reference number	PA103PCT	International application
--	----------	---------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT	
Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 1 February 1999	Accession Number 203609
C. ADDITIONAL INDICATIONS (leave blank if not applicable)	
This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only <input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US 05 MAR 2000</b> Authorized officer <b>Yolanda Harrod</b> <b>PCT/Intemat'l Appl Processing Div.</b> <b>(703) 305 667</b>	For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
---	---



**ATCC Deposit No. 203609****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 203609

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

459

Applicant's or agent's file reference number	PA103PCT	International application?
---	----------	----------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <b>American Type Culture Collection</b>	
Address of depositary institution (including postal code and country) <b>10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</b>	
Date of deposit <b>1 February 1999</b>	Accession Number <b>203610</b>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only
<input checked="" type="checkbox"/> This sheet was received with the international application
<b>RO/US 08 MAR 2000</b>
Authorized officer <b>Volanda Harrod</b> <b>PCT/Internat'l Appl Processing Div.</b> <b>(703) 305-3670</b>

For International Bureau use only
<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer

**ATCC Deposit No. 203610****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**

**ATCC Deposit No. 203610**

## **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

462

Applicant's or agent's file reference number	PA103PCT	International application number
--	----------	----------------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <p>American Type Culture Collection</p>	
Address of depositary institution (including postal code and country) <p>10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</p>	
Date of deposit <p>17 November 1998</p>	Accession Number <p>203485</p>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<input checked="" type="checkbox"/> For receiving Office use only This sheet was received with the international application <b>RO/US . 08 MAR 2000</b> Authorized officer <b>Yolanda Harrod</b> <b>PCT/Internat'l Appl Processing Off.</b> <b>(703) 305-3670</b>	<input type="checkbox"/> For International Bureau use only This sheet was received by the International Bureau on: Authorized officer
--	---

**ATCC Deposit No. 203485****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**  
**ATCC Deposit No. 203485**

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.



465

Applicant's or agent's file reference number	PA103PCT	International application?
--	----------	----------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution  American Type Culture Collection	
Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit  18 June 1999	Accession Number  PTA-252
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only <input checked="" type="checkbox"/> This sheet was received with the international application <b>RO/US 03 MAR 2000</b> Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div.	For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
--	---

**ATCC Deposit No. PTA-252****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2**

**ATCC Deposit No. PTA-252**

## **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

468

Applicant's or agent's file reference number	PA103PCT	International application N°
--	----------	------------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 18 June 1999	Accession Number PTA-253
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only <input checked="" type="checkbox"/> This sheet was received with the international application 80/US 03 MAR 2000 Authorized officer Yolanda Harrod PCT/International Appl Processing Div. (703) 305-3670	For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
--	---

**ATCC Deposit No. PTA-253****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**Page 2****ATCC Deposit No. PTA-253****DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

471

Applicant's or agent's file reference number	PA103PCT	International application number
--	----------	----------------------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>72</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <b>American Type Culture Collection</b>	
Address of depositary institution (including postal code and country) <b>10801 University Boulevard Manassas, Virginia 20110-2209 United States of America</b>	
Date of deposit <b>22 December 1999</b>	Accession Number <b>PTA-1081</b>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

<input checked="" type="checkbox"/> For receiving Office use only This sheet was received with the international application <b>RO/US 03 MAR 2000</b> Authorized officer <b>Valenda Harrod</b> <b>PCT/Internet Appl Processing Div.</b> <b>(703) 305-3670</b>	<input type="checkbox"/> For International Bureau use only This sheet was received by the International Bureau on: Authorized officer
--	---

**ATCC Deposit No. PTA-1081****CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.



Page 2

ATCC Deposit No. PTA-1081

#### **DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### **NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

*What Is Claimed Is:*

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
  - (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (c) a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO:X or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (d) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (f) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X, having biological activity;
  - (g) a polynucleotide which is a variant of SEQ ID NO:X;
  - (h) a polynucleotide which is an allelic variant of SEQ ID NO:X;
  - (i) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
  - (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide

sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

5

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

10

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

15

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

20

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

25

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

30

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least  
5 95% identical to a sequence selected from the group consisting of:
- (a) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (b) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone, having biological activity;
  - 10 (c) a polypeptide domain of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (d) a polypeptide epitope of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (e) a full length protein of SEQ ID NO:Y or of the sequence encoded by the  
15 cDNA included in the related cDNA clone;
  - (f) a variant of SEQ ID NO:Y;
  - (g) an allelic variant of SEQ ID NO:Y; or
  - (h) a species homologue of the SEQ ID NO:Y.
- 20 12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
13. An isolated antibody that binds specifically to the isolated polypeptide  
25 of claim 11.
14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
- 30 15. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

5           16.    The polypeptide produced by claim 15.

17.    A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

10

18.    A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

15           (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19.    A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

20           (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

25           20.    A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

30

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
22. A method of identifying an activity in a biological assay, wherein the method comprises:
- 5 (a) expressing SEQ ID NO:X in a cell;
- (b) isolating the supernatant;
- (c) detecting an activity in a biological assay; and
- (d) identifying the protein in the supernatant having the activity.
- 10 23. The product produced by the method of claim 20.

## SEQUENCE LISTING

<110> Craig Rosen,  
Steve Ruben

<120> Human Breast and Ovarian Cancer Associated Gene Sequences and  
Polypeptides

<130> PA103PCT

<140> Unassigned

<141> 2000-03-08

<150> 60/124,270

<151> 1999-03-12

<160> 846

<170> PatentIn Ver. 2.0

<210> 1

<211> 1913

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (944)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1418)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1908)

<223> n equals a,t,g, or c

<400> 1

ggtcanagac tggttcctgt ggtatgtgaa gaagtgtgga ggcacaacaa gaatcatctc 60  
gacaacaaat ggaggacagg agaggaaatt tgtgggcgga tctggtcaag tgagtgagcg 120  
gataatggac ctccttgagg accgagttaa gctggagagg cctgtgatct acattgacca 180  
gacaagagaa aatgtccttg tggagaccct aaaccatgag atgtatgagg ctaaatatgt 240  
gattagtgtc attcctccta ctctgggcat gaagattcac ttcaatcccc ctctgccaat 300

```

gatgagaaac cagatgatca ctctgtgtgcc tttgggttca gtcacaaagt gtatagttta 360
ttataaagag cctttctgga ggaaaaagga ttactgtgga accatgatta ttgatggaga 420
agaagctcca gttgcctaca cgttggtatga taccaaacct gaaggcaact atgctgccat 480
aatgggattt atcctggccc acaaagccag aaaactggca cgtcttacca aagaggaaa 540
gttgaagaaa ctttgtgaac tctatgcaa ggttctgggt tccctagaag ctctggagcc 600
agtgcattat gaagaaaaga actggtgtga ggagcagtac tctgggggct gctacacaac 660
ttatttcccc cctgggatcc tgactcaata tggaagggtt ctacgccagc cagtggacag 720
gatttacttt gcaggcaccg agactgccac acactggagc ggctacatgg agggggctgt 780
agaggccggg gagagagcag cccgagagat cctgcatgcc atggggaaga ttccagagga 840
tgaaatctgg cagtcagaac cagagctctg ggatgtccct gcacagccca tcaccaccac 900
ctttttggag agacatttgc cctccgtgcc aggcctgctc aggntgattg gattgaccac 960
catcttttca gcaacggctc ttggcttctt ggcccacaaa agggggctac ttgtgagagt 1020
ctaaagagag aggggtgtctg taatcacact ctcttcttac tgtatttggg atatgagttt 1080
ggggaagag ttgcagtaaa gttccatgaa gacaaatagt gtggagtga gcggggagca 1140
tgaagataaa tccaactctg actgtaaaat acatgggtatc tctttctccg ttgtggcccc 1200
tgcttagtgt cccttacctg gcttagcgtt ctgtttcacc agtttccaag tttattgccc 1260
tcaaaatctt tagaatagtt aaattggctt gtttaagggt cttgctgccc cacaacacac 1320
cttgcccatg cacaaggaat gaatttttct ctaccattat ggctttgtgc ttgttcttcc 1380
tcttacctgt aatagcctca ccttccctag ttctttgnca ttcgtcctta gaatactgta 1440
ttgttacagc tgaaagacag taaagaccat ttagtcctca cttctgttt tagagttgag 1500
caaactgaag cccacagagg tggaacttaa ttacctaaga gccacaataa gccactggta 1560
tctgggggac tagaacacaa atccaacgct tttcccacct ctttggtatg tttccccaat 1620
tctctctctt cactccctgt catagttacc gatggtgtcc cgttgtgtgg gtttactctg 1680
tgctaagttg tcttacactt ctcaaatgct actcagtata tagccttaag tcttactgtt 1740
ttgtgcggtg tgtctccagc tgattttaac ttttttgatg gttagaaattt tatctcttct 1800
tccttttgta tcctccattg tatcttcata caaaggacag tacacacttg ggtaattaaa 1860
aataaaagtt gattgaccat aaaaaaaaaa aaaggggggg ccgccangg ggg 1913

```

<210> 2

<211> 1425

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (790)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (842)

<223> n equals a,t,g, or c

<400> 2

```

acttatttat cctgcttgaa agctacttgm gatgtgtact gctattctaa acacgtgac 60
tagtttcttt catctctggc ataagattat ataacttaat gttaagtgtc ttgmggcata 120
aaagacaaaa tgtggcttat tttaggatct gttttttcat cgaggctctg ggtatccttt 180
caaagatagt garaagcaga cactgctcct tgtgcagctc tggtagctcc tgcccactgc 240
tgtcacttca agccactggc aatgcttctg tcctcgtgtc ttggaggaaa atcacctggg 300
gggagggggc ttcttgtggt aagagcaagt gcaggatga aatgcgaaga ttgccccagc 360
taaaagtgga caagtccgct ttgtgagatg aatacttcct gagaaacttg acaagtatct 420

```



```

ctccatttta ccattatgaa aactatcatt aaaaaaaca gtttagatgc cttctccttt 480
tgagggaaaa aggggtgcttt ttattgtata aagcagcgtc ttatgtattt tgatatacca 540
ttgtttgaac ttccgtcttt agctgataga ttctcaaata tccttgattt tggatgttca 600
gtatgtttgt gagagagggt tctgggaaga ctctcttttt gccctcggga aaaagcaaaa 660
tatcaatggt tgggtgactg tgtaaagctc agtgtgtaag aacatctttt tgtctaggtt 720
ttctttctgc tctttattga agacaaacac tcaccaaaaa gaaaaataaa agttttcaga 780
gaaactaata ttcyttgggc aagagtatta cytaaatatt tkggccyccy aaagttyccc 840
ynagtwagta ctcggacycc tgtgctaatt gtcagcytac atatcattgt atagagactg 900
tttawtctgt accaaactga tttcaaaagt actacattga aaataaaccg gtgactgttt 960
ttcttcataa agttctgcgt ttggcatctt cactctttcc aaaatgtatc tgtacatcag 1020
aaatgtcact attccaagtg tctttttagt gtggctttag tatggcttcc ttttaatat 1080
gtacatacat tgtatctttg ttttatggta ataagtaata aaaatgtaga cttcatattt 1140
tgtacaaaat gtcttatgta cagaataaaa aagttcatag aaacagcaaa tataggttaag 1200
tggcacaatt atttttcttt agaaaatatc tgtaacttta tgcattagtg aaatgttaag 1260
taccgacata ttttttaaca ttttgtaatt caaaactttt tgttttgaca ttgtttatga 1320
agagaaactt catacacttg ccatttaata tgctctttta tctaattttc aaaaactcta 1380
aaaaacggtg tatcatatgg actaaataaa gaacatgtga atttt 1425

```

&lt;210&gt; 3

&lt;211&gt; 354

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (246)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 3

```

ggcacgagaa ccatttccac tatatatctc ttcggataac taraaattaa awtatttggt 60
gtattatttg caaggagtca aagatgatgt cttttcccag aggcattgaac cttagaatag 120
ctttcgatgg ggatgtttct gtaacactgt gttattctgg atcttcaaata aatagcaaaag 180
ccaattactc taaatgtaaa atttttctat tcccaagggt cacttttggt tggtaggttt 240
tcacgntttt aaatactggt taatggaaga aaaatacgta gccaggcgtg gtggctcaca 300
cctgtagccc cggaactttg ggagactgaa gcgggcagat cagaggtca ggag 354

```

&lt;210&gt; 4

&lt;211&gt; 514

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (502)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 4

```

agacgcacgc gtactgctcc aacctcagct tccgcctcta cgaccagtgg cgagcctgga 60
tgcagaagtc gcacaagacc cgcaaccagc acaggacgag gggatcctgc cctcgggcag 120
acggggcacg gcgagaggtc ctgccagata agctgtaggg gctcaggcca cctccctgc 180
cacgtggaga cgcagaggcc gaacccaaac tggggccacc tctgtaccct cacttcaggg 240

```

```

cacctgagcc accctcagca ggagctgggg tggccctga gctccaacgg ccataacagc 300
tctgactccc acgtgaggcc acctttgggt gcacccagtg ggtgtgtgt gtgtgtgtga 360
gggttggttg agttgcctag aaccctgcc agggctgggg gtgagaagg gagtcattac 420
tccccattac ctaggggccc tccaaaagag tccttttaaa taaatgagct atttaggtgc 480
wraaaaaaaa aaaaaaaaaac cncggggggg gcc 514

```

&lt;210&gt; 5

&lt;211&gt; 2035

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 5

```

cacgaggaat gacatgaaag cagactgtat tttgtactac ggctttggag atatattcag 60
aataagttca atggtggtga tggaaaatgt gggacagcag aagctttatg agatggtatc 120
atactgtcaa aacataagca aatgtcgtcg tgtgttgatg gctcaacatt ttgatgaagt 180
atggaactca gaagcatgta acaaaatgtg cgrtaactgc tgtaaagaca gtgcatttga 240
aagaaagaac ataacagagt actgcagaga tctaatacag atcctgaagc aggcagaggg 300
amctggaatg gaaaaactca ctcccattgg aaactggatt gattcttggr tgggaaagg 360
tgcagcaaaa ctgagagtag caggtgttgt ggctcccaca ctctctctg aagatctgga 420
gaagattatt gcacacttts taatacagca gtatcttaaa gaagactaca gttttacagc 480
ttatgctacc atttcgtatt tgaaaatagg acctaaagct aatcttctga acaatgaggc 540
acatgctatt actatgcaag tgacaaaagc cacgcagaac tctttcaggg ctgaatcgtc 600
tcaaacttgt cattctgaac aaggtgataa aaagatggag gaaaaaaatt caggcaactt 660
ccagaagaag gctgcaaaaca tgcttcagca atctggttct aagaatacag gagctaagaa 720
aagaaaaatc gatgatgcct gatatgaatg ttactaaatt ttctaattaa agatggttta 780
tgcatgtata tgccattatt tttgtagtta gacaatagtt tttaaaagaa tttcatagat 840
attttatatg tatggatcta tttttcaga gcttatctct gaagatctaa acttttgaga 900
atgtttgaaa attagagatc atgaattata taattttcca gtataaaaca agggaaaaat 960
tttatgttaa aaccttttaa atgtaaaata ttgagaata agttcataca atcgtcttaa 1020
gttttttatg cctttatata cttagctata ttttttcttt tgacataact atctttttga 1080
aagcaatatt atactgacag aggcctactg agtgataact taagttaaat atgtagatca 1140
aggatgtcca atcttttggc ttccctgagc cacattggaa gaagaattgt cttggggccg 1200
acataaaata tgctaacact gatgatagct gatgagctta aaaaaaaat tgcaagaaaa 1260
atctcatgtt ttaagaaagt ttacaaaaaa tgtaaaatat ttgagaataa gttcatgtaa 1320
ttgtcttaag ttttttatgc ctttatatac ttagctatat tttttctttt gacataacca 1380
tctttttgaa agcaatatta tactgacaga ggytcaactga gtgatacttt aagttaaata 1440
tgtagatcag ggatgtccaa tcttttggct tccctgagcc acattggaag aagaattgtc 1500
ttgggccgca cataaaatat gctaacactg acgatagctg atgagcttaa aaaaaaaaaa 1560
attgcaagaa aaatctcatg ttttaagaaa gtttacagat ttgtgttggg ctgcattcaa 1620
agctgttctg ggctgcatta gaccctggg ctgaggttg acaagcttgt agatgatttc 1680
aggttataaa accagaagta caattcaaca aaaaaggagt aagtcacaa tataaatatt 1740
agcaaacgag atattgctac atctctatct aaagtaaaat acaaccgatt ttaaagttcc 1800
tgaaaccata gccatatttt gacatttcac aaagaatggt tctagtctac tagagtacat 1860
ttggctaagt agataactta cctaaatttg ctccaaagct aaatcacaa taaacatatt 1920
tatgttttaa acacagaaat aaataactta agatttttat ctaagcggtc agtgttgtrt 1980
tggaaagata tatctataaa taaactttga actgatttca aacttaaaaa aaaaa 2035

```

&lt;210&gt; 6

&lt;211&gt; 1196

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<220>  
 <221> misc feature  
 <222> (157)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (998)  
 <223> n equals a,t,g, or c

<400> 6  
 ggtgggtgtg ggactggggg ctgtgagtgt gagtgtgtgc aagagattgc tctgcatgtt 60  
 tgctgagggc tggagctggg cttttcagag atcgggcac cctgggtctct cagggccagt 120  
 tggaggttcc caggaggcat gttcttgatg cctgtgntgc ctgaatccaa ttaactgaat 180  
 tctgaagagt gcatggggta actgtctcag ctttctcct gtctctgcct ctgtcctctg 240  
 ctccaaatca taaaatctca gagctagaag cactttcaag atcattccat ccagcgcat 300  
 caatttgcaa gtttaggcgt tgagttccag agagggatgg tagcttgctg aggtcccagt 360  
 caagcacact tgccattgcc tcagctttcc cctaaacacg gtgtctgtgg tcagggttgg 420  
 tgaggaggag ctttctgtt ttgcctctcc ttcttccat tggctacacc catctytggc 480  
 cctgctgata ccgattcccc tgacatttca ggctaaagcc agcaggraag ggctagggac 540  
 ggggtgcctg gaagcccaca tggaggaggt tggcaagat ttgattcgga gcaggtgtca 600  
 agacgtgttg gggaaactga ggcccagtgg aatagaagcc agtagaggag gaatctagag 660  
 gcctcctaga ttaaggcctg cctggaatgg attgggggtg ggtctttgga aaaggagggg 720  
 acccacctct agcccagtct ctcaactgcc cctcctttac agtgagttag atcattggcc 780  
 gagacctgag tggcttccct gcacctctg gagaagagcc tctgcctga accacgtgaa 840  
 ctgtcatcac ctggcaaccc cagcccagc ctcagccctg cccctttcc ctccttctg 900  
 gagtgggtggc tacagaagct tggggccaac cctggctcct ctttccccag cttctgtctg 960  
 tctcactgtc tcccctcccc tccccagct gaggtgtngc cctcaggcct ggtgctgcct 1020  
 tggagggtctg ggggaaggag tgtgtggagg agggaggagg gtgaagactg aggttaggtg 1080  
 ccagaatgga ctggagtga ggcgtgtcta gagtgtgggc tggctgtgtg gctggaaagc 1140  
 tggggacagg ttgatggtaa taaactgctc aatgaccagt gaaaaaaaa aaaaaa 1196

<210> 7  
 <211> 624  
 <212> DNA  
 <213> Homo sapiens

<400> 7  
 attatatttca agtcaaaatt tccagtaagg atttacttta catttcattt ggataaatga 60  
 atcattatat aggtatgtct ttgcttccat tttgagacat ttagattttt acagcctgtt 120  
 tctatagcat ttgatgttac aactctaagc gtagtccaag gacatttaaa ttgacaagtt 180  
 accagttaaa gaatttagaa tatattagat cccatctagt attatatatt ttttctagtt 240  
 gatcattgag cagtaaaatac caaatactcg attagaaggt aatttttaca ttgttttgaa 300  
 aggggtgaamc aatttatctc ctctgggtatt attcttaaac cacagatagg gatagtaggg 360  
 tagtgaaacg mataaatacc tggtagaaga caagagactt gggctctaca cctggctctg 420  
 cactgatttg ctaagtcata ttggcaatca ccacaccctt cagggaatta gtttcatctg 480  
 taaaatgcag cggttagtac tatwaaatca tacmaatttc tttgtgcttt gagaatctwt 540  
 aarggaatgt ctgttgatat tctgagtcga ttttcatttg cttttgttcc agaacggtta 600  
 aaataaagca tattatttca tttta 624

<210> 8  
 <211> 301  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (289)  
 <223> n equals a,t,g, or c

<400> 8  
 aattcggcac gagcggcgac ggcgggcggt ccaagatggc gcaggcgatc tttgaggccc 60  
 tggagggaat ggacaatcag accgttcttg ctgtccagtc attattggat ggccaaggag 120  
 cagtccctga tccgacaggc cagagtgtca atgcgcccc tgctatccag ccattggatg 180  
 acgaggatgt atttctctgc gggaagtgt agaagcaatt caactcgctg ccagcgttta 240  
 tgaccacaa gcgggaacag tgccagggga atgccccgc cctggccana gtctactg 300  
 c 301

<210> 9  
 <211> 686  
 <212> DNA  
 <213> Homo sapiens

<400> 9  
 acccacgct cgcgccaact cctctttcgt ctttctttaa cacacactag gctctttgtg 60  
 tattatgatt cagtgtatt tgtaactgtg tcccagtgac caaattgcac tcgactcgat 120  
 cagctgttca tccatttcgt gttttttcct gtcaaacatt aatccagcaa atatatgagg 180  
 tatttaccaa tttattttct tagtattaca aaataattca ttagcataaa gtacaatagt 240  
 gaaatatttg agtggttcgg aacctcaatt aatcctgttt tacatttcag acctaaagct 300  
 ggcaatcagg agaagaagca ctttgtttta aatgtggaga agataacacc ttgattccat 360  
 ttcattgtca ttagtgtatt aaccagcagg agagtgatg agccattttt caaatgaaat 420  
 accttttatt tccatataat ttttttattt tagagttcaa tagctgtttc tatgattatc 480  
 ctcaatttcc atatgttact gaatctgaaa aacatcttta aaattcaaac agttccattt 540  
 tctctcttgt aagtgttaaa tgtgataaaa gtacatattt taaattgttt tcagctcttg 600  
 gatatagcag caataaaaac actaatttgt gggtatttaa gaaaacctgg agaataaaact 660  
 catactttaa aagatcaaaa aaaaaa 686

<210> 10  
 <211> 397  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (379)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (394)  
 <223> n equals a,t,g, or c

```

<400> 10
cacacgctta gcaacctgga gtttgcccag aaagtggagc cctgcaacga ccacgtgaga 60
gccaaagctgt cctgggctaa gaagagggat gaggatgacg tgcccactgt gccgtcgact 120
cygggcgagg agcgcctcta caacccttc ctgcgggtgg cgtgagtatg gctgttgctc 180
cggggcctcc accgttacgt ggacccttag gaaggcatct ggggactgcg tgttgggctg 240
agtgagcatc tctggcttgg gggaggctgc tcattaagtg cctgcctgcc cgscamccc 300
tcggcgccat gctcccgcgt gggcagcggg cctgcgccct cactgcaccc ctccctgcag 360
agaggagccg gtgcgcaant ttcacgggca aggnnggt 397

```

```

<210> 11
<211> 563
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (10)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (13)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (37)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (510)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (562)
<223> n equals a,t,g, or c

```

```

<400> 11
aggcaaaacn gtnagaccga cagtaaccgg atccggnaat tcccgggtac gacccacgcg 60
tccggatata tcagagtaac tggagtagct gggatttact agtagtgtaa ataaaattca 120
ctcttcaata catgaatgga aacttaaatt ttttttttat gtgtccttgc ttatagttta 180
gctgtaataa ttttaacctg tattcttggt ccatattctg tctttttatt acttataaag 240
acaaacccaa gtaaatctga aggagacyag aagctttgaa attattgttt gggggtttta 300
taaaagcaac tactgtcacc tccatccaga ttcttttaaa ttattgatcc atccatagta 360
tatattgcta ctcatccaag aatcctcaat aagtattgag tatttaccat atgttgggat 420
actgtgggct ctggagagag gagggggcaa tagagctagg rattaaggaa tcagttgwtg 480
aaaatgkgt atattttatc ccccattaan taactggact aggggaaggga ctaaaaggcc 540
agaaaggggg atgaaaaaaa ant 563

```

<210> 12  
 <211> 443  
 <212> DNA  
 <213> Homo sapiens

<400> 12  
 gagacctcgg ctccggaatc actgcagccc ccctcgccct gagccagagc accccggggtc 60  
 ccgccagccc ctcacactcc cagcaaatg ggcaaggaga agaccacat caacatcgtg 120  
 gtcacgagcc acgtggactc cggaaagtcc accaccacgg gccacctcat ctacaaatgc 180  
 ggaggtattg acaaaaggac cattgagaag ttcgagaagg aggcggctga gatggggaag 240  
 ggatccttca agtatgcctg ggtgctggac aagctgaagg cggasgtgag cgcgrrcatc 300  
 accatcgaca tctccctctg gaagttcgag accaccaagt actacatcac catcatcgat 360  
 gcccccgccc accgcgactt catcaagaac atgatcacgg gtacatccca ggcggactgc 420  
 gcagtgtga tcgtggcgcc ggg 443

<210> 13  
 <211> 2438  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (117)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (681)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (713)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (2413)  
 <223> n equals a,t,g, or c

<400> 13  
 cactgggagg ggggtgggga tctgggcaag gtgggtgatt cctcccagga ggtgcttgag 60  
 gccccgatgg actcctgacc ataatectag ccccagagaca ccacctgag ccagggnaac 120  
 agccccaggg ttgggggggtg ccggcatctc ccctagctca ccaggcctgg cctctgggca 180  
 gtgtggcctc ttggtattt ctgtgtccag ttttggaggc tgagttctgg ttcatgcaga 240  
 caaagccctg tccttcagtc ttctagaaac agagacaaga aaggcagaca caccgcggcc 300  
 aggcacccat gtgggcgccc accctgggct ccacacagca gtgtcccctg ccccaragg 360  
 cgcagctacc ctcagcctcc aatgcattgg cctctgtacc gcccggcagc cccttctggc 420  
 cgggtgtggg ttccactcc cggcctaggc acctccccgc tctccctgtc acgstcatgt 480  
 cctgtcctgg tcctgatgcc cgttgtctag gagacagagc caagcactgc tcacgtctct 540

```

gccgcctgcg tttggaggcc cctgggctct caccagttcc ccaccgcct gcagagaggg 600
aactagggca ccccttggtt ctgttggtcc cgtgaatttt ttctgctatg ggaggcagcc 660
gaggcctggc caatgcggcc nactttcctg agctgtcgct gcctccatgg canagccarg 720
gacccccaga acaagaagac cccccgcag atccctcctg agctcggggg gctctgcctt 780
ctcaggcccc gggtttccct tctccccagc cagaggtgga gccaaagtgt ccagcgtcac 840
tccagtgtct agctgtggct ggaggagctg gcctgtggca cagccctgag tgtcccaagc 900
cgggagccaa cgaagccgga cacggcttca ctgaccagcg gctgctcaag ccgcaagctc 960
tcagcaagtg cccagtggag cctgccgccc ccrcctgggc accgggaccc cctcaccatc 1020
cagtgggccc ggagaaacct gatgaacagt ttggggactc aggaccagat gtccgtctct 1080
cttgcttgag gaatgaagac ctttattcac ccctgccccg ttgcttcccg ctgcacatgg 1140
acagacttca cagcgtctgc tcataggacc tgcatccttc ctggggacga attccactcg 1200
tccaagggac agcccacggt ctggaggccg aggaccacca gcaggcaggt ggactgactg 1260
tgttgggcaa gacctcttcc ctctgggccc gtctctcttg ctgcaaataa ggacagcagc 1320
tggtgcccc actgcctggt gcattgctgt gtgaatccag gaggcagtg acatcgtagg 1380
cagccacggc cccgggtcca ggagaagtgc tccctggagg cagcaccac tgcttccac 1440
tggggccggc gggggccacg cacgacgtca gcctcttacc ttcccgcctc ggctaggggt 1500
cctcgggatg ccgttctgtt ccaacctcct gctctgggac gtggacatgc ctcaaggata 1560
cagggagccg gcggcctctc gacggcacgc acttgctgtg ttgctgctgc ggctgtgggc 1620
gagcatgggg gctgccagcg tctgttggtg aaagtagctg ctagtgaat ggctggggcc 1680
gctggggtcc gtcttcacac tgcgcaggtc tcttctgggc gtctgagctg ggggtggagc 1740
tcctccgcag aagggttggtg ggggttccag tctgtgatcc ttggtgctgt gtgccccact 1800
ccagcctggg gacccactt cagaaggtag ggccgtgtc ccgcggtgct gactgaggcc 1860
tgcttcccc tccccctcct gctgtgctgg aattccacag ggaccagggc caccgcaggg 1920
actgtctcag aagacttgat ttttcgctc ctttttctcc aactccact gacaaacgtc 1980
cccagcgtt tccacttggt ggcttcaggt gttttcaagc acaaccacc acaacaagca 2040
agtgcatttt cagtcgttgt gctttttgt tttgtgctaa cgtcttacta atttaaagat 2100
gctgtcggca ccatgtttat ttatttccag tggtcatgct cagccttgct gctctgcgtg 2160
gcgcaggtgc catgcctgct ccctgtctgt gtcccagcca cgcagggccca tccactgtga 2220
cgtcggccga ccaggctgga caccctctgc cgagtaatga cgtgtgtggc tgggaccttc 2280
tttattctgt gttaatggct aacctgttac actgggctgg gttgggtagg gtgttctggc 2340
ttttttgtgg ggtttttatt tttaaagaaa cactcaatca tcctaaaaaa aaaaaaaaaa 2400
aaaaaaaaaa ttntctcggtc cgcaagggaa ttcagtgg 2438

```

&lt;210&gt; 14

&lt;211&gt; 2347

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 14

```

aattcggcac gmgctgagga ccgcacggaa acggggaagt cagggtggccg ctgccgccgc 60
cgccgccgcg gtttgctgcc agaaggaaga tggcggatct ggaggagcag ttgtctgatg 120
aagagaaggt gcgtatagca gaaaattca tcattcatgc ccctcctgga gaatttaatg 180
aggttttcaa tgatgttcgg ttactgctta ataatgaaa tcttctcagg gaaggagcag 240
cccatgcatt tgcacagtat aacttgacc agtttactcc agtaaaaatt gaaggttatg 300
aagatcaggt attgataaca gaacatggcg acttgggaaa tggaaagttt ttggatccaa 360
agaacagaat ctgttttaaa ttgatcact taaggaagga ggcaactgat ccaagaccct 420
gtgaagtaga aaatgcagtt gaatcatgga gaacttcagt agaaactgct ctgagagctt 480
acgtaaaaga acattacccg aatggagtct gcactgtgta tggcaaaaaa atagatggac 540
agcaaacat tattgcagtc atagaaagcc atcagttcca agcaaaaaat ttttggaatg 600
gtcgttgag gtcagaatgg aagtttaca tctctcttc aaccactcaa gtggttgga 660
tcttgaaaat tcaggttcat tattatgaag atggtaatgt tcagctagtg agtcataaag 720

```

```

atatacaaga ttccctaaca gtgtctaata aagtgcacaa agcaaaagaa ttataaaga 780
ttgtagaagc tgcagaaaat gaataccaga ctgccatcag tgagaattat cagacaatgt 840
cggacactac tttcaaagcc ttacgtcgac agttgccagt tacacgcact aagattgatt 900
ggaacaagat ccttagctac aagattggca aagagatgca gaatgcataa gatgaacatt 960
gcatgaccgg atcatttttag tgtctttgag ttaaaaaatc attgcaaaag tattctgaac 1020
tgtcaagctg cccagtcaga tgggctgttg ccatttaaaa tcaactgtaat taattagttt 1080
gattagagca caaagccttag ctaatcaacc attatttttc attttggttg ttctaagagg 1140
attgaaaatc agtttagttt aaatgtcttt ctgtaggccc tttctttctt acaatgaaga 1200
gatgattctt ctagtttatg gttaaaagtt tttgaagtgt ctcaaaaata ttttactaac 1260
tgtaacccta aaattgatgt cttttgggtt atgaaatcag taatttttga ttttcccca 1320
gttcttttta atgggggtcaa taatggacat tcttctctca cctgttccat ttatgtaaag 1380
atatatgctg ctaaaagaaat tgtctacctt ttcttctctca cctgttccat ttatgtaaag 1440
ttgagattag agggaaaagca ttttctatat caattgtgtt taaacctttc aagaagggtta 1500
tttagctagc ttagtgttga actaaatttt ttttaaacaa ggcaaggtct aatgctgttt 1560
tgagattctg aaattaatga aaatacttat ttcagaaatg catttaatgc tttttttctt 1620
gtgacagtta cgcaaatcag cttgaattcc atatgtccct gagttatttt tatcataaag 1680
ccacaaatgt attataacaa ggcaaatgt aatatatata atcctgaact catgaccatg 1740
tctcggttta tttttttttt cttggattga aaagtactga aattcaatgt gacattaaaa 1800
tgcaaatttt cctattttat tgagtagaaa atcacttacc agtgagcata tatattttta 1860
aatactttct ttggatattg taattcttaa ctgggtgtta attagaaaag ctgggattac 1920
atatgggtgt cggttacagt ctaaattttt tcatcctcct atgcatcata agcatgtttg 1980
taatattttc aaaaatagtt ctactgatgc tacaggaatt tcaagcctgt ggtgaatgtt 2040
agtattttacc atagggagtg aagtggagtt atgggttcat tcaatagagt attgcygatt 2100
atacttgagt ggaatccttt cctcacgtac tcccacagac gtctgggcct ggaaattttt 2160
tttttatttt attttattgt tttttttttt agaaaaacac cacttttatt atgtacaata 2220
aaatatttca ttagcttgaa ttgtatagat ttttaaaaaat tcaatgaaag catgttggtt 2280
aatttctttt taaaatcact gttgggcttt gaaagcattg agaataata atgaaattat 2340
gaaaaaa 2347

```

<210> 15

<211> 2006

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (862)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1006)

<223> n equals a,t,g, or c

<400> 15

```

ggcagagctg taccagtggc agcagcaagc cgaatagccc cagcatttcc cttcaatac 60
ttagtaaacac ggagcacaaag aggggacctg aggtcacttc ccaaggggtt cagacttcca 120
gcccagcatg taaacaagag aaagacgata aggaagagaa gaaagacgca gctgagcaag 180
ttaggaaatc aacattgaat cccaatgcaa aggagttcaa cccacgttcc ttctctcagc 240
caaagccttc tactacccca acttcacctc ggcctcaagc acaacctagc ccatctatgg 300
tgggtcatca acagccaact ccagtttata ctcagcctgt ttgttttgca ccaaatatga 360

```



```

tgtatccagt cccagtgagc ccaggcgtgc aacctttata cccaatacct atgacgcca 420
tgccagtga tcaagccaag acatatagag caggtaaagt accaaatatg ccccaacagc 480
ggcaagacca gcatcatcag agtgccatga tgcaaccagc gtcagcagcg ggcccaccga 540
ttgcagcmac cccaccagct tactccacgc aatatgttgc ctacagtcct cagcagttcc 600
caaatcagcc ccttgttcag catgtgccac attatcagtc tcagcatcct catgtctata 660
gtcctgtaat acagggtaat gctagaatga tggcaccacc aacacacgcc cagcctggtt 720
tagtatcttc ttcagcaact cagtacggg ctcatgagca gacgcagcg atgtatgcat 780
gtcccaaat accatacaac aaggagacaa gcccttcttt ctactttgcc atttccacgg 840
gtcccttgc tcagcagtat gngcracct aacgctacce tgcaccaca tactccacac 900
cctcagcctt cagctacccc cactggacag cagcaaagcc aacatggtgg aagtcaccc 960
gcaccagtc ctgttcagca ccatcagcac caggccgccc aggctnctcc atctggccag 1020
tccacagcag cagtcagcca tttaccacgc ggggcttgcg ccaactccac cctccatgac 1080
acctgcctcc aacacgcagt cgccacagaa tagtttccca gcagcacaac agactgtytt 1140
tacgatccat ccttctcacg ttcagccggc gtataccaac ccaccccaca tggcccacgt 1200
acctcaggct catgtacagt caggaatggt tccttctcat ccaactgcc atgcgccaat 1260
gatgctaata acgacacagc caccggcggt tccccaggcc gccctcgctc aaagtgcact 1320
acagcccatt ccagtcctga caacagcgca ttccctctat atgacgcacc cttcagtaca 1380
agcccaccac caacagcagt tgtaaggctg ccctggagga accgaaaggc caaattccct 1440
ctcccttct actgcttcta ccaactggaa gcacagaaaa ctagaatttc atttattttg 1500
tttttaaaat atatagtgtg atttcttgta acatccaata ggaatgctaa cagttcactt 1560
gcagtggaa atacttggac cgagtagagg catttaggaa cttgggggct attccataat 1620
tccatatgct gtttcagagt cccgcaggta cccagctct gcttgccgaa actggaagtt 1680
atttattttt taataaccct tgaaagtcac gaacacatca gctagcaaaa gaagtaacaa 1740
gagtgtattc tgctgtatt actgctaaaa aaaaaaaaaa aaaaaaatca agacttgga 1800
cgccctttta ctaaacttga caaagtttca gtaaattctt accgtcaaac tgacggatta 1860
ttatttataa atcaagttg atgaggtgat cactgtctac agtggttcaa cttttaagtt 1920
aagggaaaaa cttttacttt gtagataata taaaataaaa acttaaaaaa aatttaaaaa 1980
ataaaaaaag ttttaaaaac tgaaaaa
2006

```

<210> 16

<211> 986

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (613)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (932)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (933)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (985)

<223> n equals a,t,g, or c

<400> 16

```
tcaaagtaac tctgacctc aagccaacag aagcctcaag ttcggctttt cgcttgatgc 60
cagctcttgg cgtgagtgtg gctgaccaga agggaaaaag cacagtggcc tcttcagaag 120
caaaaccagc tgccacgata cgcatcgtgc agggactggg agtgatgcct cccaaagcag 180
gccagaccat caccgttgca acccacgcca agcaaggggc ctcggtggcc agtgggtctg 240
gaactgtcca tacttcagcg gtgtccttac ccagtatgaa tgctgctgtg tccaagactg 300
tagctgtggc ttctggggct gcaagacccc catcagcatc agcacaggag cccccaccgt 360
gcggcaggtc cctgtcagca ccacggttgt gtccacgtcc caggctggga agttgcctac 420
acggatcaca gttccctctc ctgtgatcag ccagccaatg aagggcaaga gcgtgggtcac 480
agccccatc atcaaaggca accttgagc caacctcagt gggttgggccc gcaacatcat 540
cctcacaact atgccagcag gactaagct cattgctggc aataagcctg ttagtttcct 600
cactgctcag canttgacg agcttcagca gcaagggtcag gccacacagg tgcgcatcca 660
gactgtccct gcatcccatc tccaacaggg aacagcttct ggctcctcca aagcagtctc 720
cactgttgtt gtgactacag ctccgtctcc taaacaggca cctgagcaac aatgattatg 780
agagaggatg gcttccgtga aagaccatgc ctggtctgtc ctggctgaga agggaccagg 840
gagttgcatc attgttttaa gctgcctgtt caaggcagcc aggcgagggt gatggcaacg 900
gtggcctggt tygtgggcct ggattctgcg cnngggccat agtgggagca ccctgagaaa 960
ggtcactccc gggttccaaa ggctng 986
```

<210> 17

<211> 1589

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (25)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (555)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (809)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1033)

<223> n equals a,t,g, or c

<400> 17

```
tttgaacttg gggaaacaag gttgncatcc cagtggcctc aaccctccct cagcccctct 60
tgccccccac ccagcctaa gatgaagagg atcggaggct tgtcagagct gggaggggtt 120
ttcgaagctc agcccacccc cctcattttg gatataggtc agtgaaggcc caggagaggg 180
```

```

ccatgattcg cccaaagcca gacagcaacg gggaggccra gtgcaggctg gcaccgcctt 240
ctctaaatga ggggcctcag gtttgctga gggcgagggg aggggtggcag gtgaccttct 300
gggaaatggc ttgaagccaa gtcagctttg ccttccacgc tgtctccaga cccccacccc 360
ttccccactg cctgcccacc cgtggagatg ggatgcttgc ctagggcctg gtccatgatg 420
gagtcagggt tggggttcgt ggaaaggggt ctgcttccct ctgcctgtcm ctctcaggca 480
tgcctgtktg acatcagtg catggctcca gtctgctgcc ctccatcccc acatggaccc 540
ggagctaaca mtggncccct agaatcagcc taggggtcag ggaccaagga cccctcamct 600
tgcaacacac agacacamgc acacacacac acaggaggag aaatctcact tttctccatg 660
agttttttct cttgggctga gactggatac tgcccggggc agctgccaga gaagcatcgg 720
aggggaattga ggtctgctcg gccgtcttca ctgcggcccg ggtttggcgg gccaaaggact 780
gccgaccgag gctggagctg gcgtctgtnt tcaagggctt acacgtggag gaatgctccc 840
ccatcctccc ctccctgca aacatggggt tggctggggc cagaaggttg tgatgaagaa 900
aagcggggcca gtgtgggaat gcggcaagaa ggaattgact tcgactgtga cctgtgggga 960
tttctcccag ctctagacaa ccctgcaaag gactgttttt tcctgagctt ggccagaagg 1020
gggccatgag gcntcagtg actttccacc cctccctgg cctgttctgt tttgcctgaa 1080
gttgaatga gtgtggctcc cctctattta gcatgacaag ccccgagcag gctgtgcgct 1140
gacaaccacc gctccccagc ccagggttcc cccagccctg tggaaggag taggagcact 1200
gtagtaaatg gcaattcttt gacctcaacc tgtgatgagg ggaggaaact cacctgctgg 1260
cccctcacct gggcacctgg ggagtgggac agagtctggg tgtatttatt ttctcccca 1320
gcagggtggg agggggtttg ggggcttgca agtatgttt agcatgtgt tggttctggg 1380
gccccttttt actcccctt agctgagatg gaaccctttt tgtgcccgag ctgggggcca 1440
tgagctccag acccccagca accctcctat caccctccc ccttgccctc tgtgtaatca 1500
tttcttgggc cctcctgaaa cttacacaca aaacgttaag tgatgaacat taaatagcaa 1560
agaaagaaaa ataaaaaaaa aaaaaaaaaa 1589

```

<210> 18

<211> 846

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (746)

<223> n equals a,t,g, or c

<400> 18

```

gcaccgcct cgcccgatg gccaccgcag acccagctcc ccgggcagcc ggcccagccc 60
gcgcccattg tgccactgca ccagaagcag agccgcacat ccccatcca gaagccgcgg 120
ggcstcgacc ctgtggagat cctgcaggag cgcgagtaca ggctgcaggc tcgcatcgca 180
caccgaattc aggaacttga aaaccttccc ggggtccctg ccggggattt gcgaacccaa 240
gcgaccattg agctcaaggc cctcaggctg ctgaacttcc agaggcagct gcgccaggag 300
gtggtggtgt gcatgcggag ggacacagcg ctggagacag ccctcaatgc taaggcctac 360
aagcgcasaa gcgccagtc ctgcgcgagg ccgcacatcac tgagaagctg gagaagcagc 420
agaagatcga gcaggagcgc aagcgcgggc agaagcacca ggaatacctc aatagcattc 480
tccagcatgc caaggatttc aaggaatatc acagatccgt cacaggcaaa atccagaagc 540
tgaccaaggc agtggccacg taccatgcca acacggagcg ggagcagaag aaagagaacg 600
agcggatcga gaaggagcgc atgcggaggc tcatggctga agatgaggag gggtagcgca 660
agctcatcga ccagaagaag gacaagcgcc tggcctacct cttgcagcag acagacgagt 720
acgtggctaa ctcacggagc tggtgncggc acaaggctgc ccaggtcgcc aaggagaaaa 780
agaagaaaaa gaaaaagaag aaggcagaaa atgcagaagg acagacgcct gccattgggc 840
cggatg 846

```

<210> 19  
<211> 2192  
<212> DNA  
<213> Homo sapiens  
  
<220>  
<221> misc feature  
<222> (115)  
<223> n equals a,t,g, or c  
  
<220>  
<221> misc feature  
<222> (2106)  
<223> n equals a,t,g, or c  
  
<220>  
<221> misc feature  
<222> (2118)  
<223> n equals a,t,g, or c  
  
<220>  
<221> misc feature  
<222> (2143)  
<223> n equals a,t,g, or c

<400> 19  
aaacaaaagg cgatattctg cctgggcaaa tctgtgacta atcttcctca agtcataaaa 60  
caaaagctga cacctttata tgagctggta aaggaagtac cttgtgcctc tgtgnaaaaa 120  
actatacctg aaatgggctc ttgaagagta tctggatgaa tttgaccctc gtcattgccg 180  
gccttgctca aatggtgggt tggtactgtg tgaggggacc cattgtctgt gccattgcaa 240  
accgtacaca tttggtgctg cgtgtgagca aggagtcctc gtagggaatc aagcaggagg 300  
ggttgatgga gggtggagtt gctggtcctc ttggagcccc tgtgtccaag ggaagaaaac 360  
aagaagccgt gratgcaaka acccacctcc cagtgggggt gggagatcct gcgttgga 420  
aacgacagaa agcacacaat gcgaagatga ggagctggag cacttgagggt tgctgaacc 480  
acattgcttt cctttgtctt tggttccaac agaattctgt ccatcacctc ctgccttgaa 540  
agatggattt gttcaagatg aaggtacaat gtttcctgtg gggaaaaatg tagtgtacwc 600  
ttgcaatgaa ggatactctc ttattggaaa ccagtgggcc agatgtggag aagatttacg 660  
gtggcttggt ggggaaatgc attgtcagaa aattgcctgt gttctacctg tactgatgga 720  
tggcatacag agtcaccccc aaaaaccttt ctacacagtt ggtgagaagg tgactgtttc 780  
ctgttcagggt ggcattgtcct tagaagggtcc ttcagcattt ctctgtggct ccagccttaa 840  
gtggagtcct gagatgaaga atgcccgtctg tgtacaaaaa gaaaatccgt taacacaggc 900  
agtgcctaaa tgtcagcgct gggagaaact gcagaattca agatgtgttt gtaaaatgcc 960  
ctacgaatgt ggaccttcct tggatgtatg tgctcaagat gagagaagca aaaggatact 1020  
gcctctgaca gtttgcaaga tgcattgtct ccactgtcag ggtagaaatt acacccttac 1080  
tggtagggac agctgtactc tgccctgcctc agctgagaaa gcttggtgtg cctgcccact 1140  
gtggggaaaa tgtgatgctg agagcagcaa atgtgtctgc cgagaagcat cggagtgcga 1200  
ggaagaaggg tttagcattt gtgtggaagt gaacggcaag gagcagacga tgtctgagt 1260  
tgaggcgggc gctctgagat gcagagggca gagcatctct gtcaccagca taaggccttg 1320  
tgctgcggaa acccagtagg ctctggagg ccmtggtcag cttgcttgga atccagcagg 1380  
cagctggggc tgagtgaata catctgcaca actgggcact ggacagcttt tccttctcca 1440

```

gtgtctacct tctcctctcaa ctcccagcca tctgtataaa cacaatcctt tgttctccca 1500
aatctgaatc gaattactct tttgcctcct ttttaatgtc agtaaggata tgagcctttg 1560
cacaggctgg ctgctgtgtc ttgaaatagg tgttaccttc tctgggcctt ggtttttttaa 1620
aatctgtaaa attagaggat tgcactagag aaacttgaat gctccattca ggcctatcat 1680
tttattaagt atgattgaca cagcccatgg gccagaacac actctacaaa atgactagga 1740
taacagaaag aacgtgatct cctgattaga gaggttggtt ttcctcaatg gaaccaaata 1800
taaagaggac ttgaacaaaa atgacagata caaactatct ctatcctgag tagtaatctc 1860
acacttcac ctagatagtc aaccaccaca gataggratt ccttattctt tttttaatct 1920
ttttaagaca gagtctcact ttgttgccca ggytggagcg cagtggggtg atctcatctc 1980
cctgcaacct cgcctcctg ggttcaagcg attcttgtgc ctacgcttcc caagcagctg 2040
gggattacag gtgcccgcga ccacgccag ctaatttttg catttttagt agagatgggg 2100
tttcancatg ttggccangc tcgtctccaa ctctgacct cangtaatcc gcctgccttg 2160
gcctcccaaa gtgctgggat acagacatga ac
2192

```

<210> 20

<211> 1011

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (54)

<223> n equals a,t,g, or c

<400> 20

```

ctctaatacg actcactata ggcaaagctg gtagcctgca gtaccggats crgnaattcc 60
cggggatgga agcgtttttg gggctgcggt ccggactttg ggcggggggt ccggccccag 120
gacagtttta cgcattccr tccactcccg attccttcat ggatccggcg tctgcacttt 180
acagaggtcc aatcacgcgg acccagaacc ccatggtgac cgggacctca gtcctcggcg 240
ttaagttcga gggcggaagt gtgattgccg cagacatgct gggatcctac ggctccttg 300
ctcgtttccg caacatctct cgcattatgc gagtcaacaa cagtaccatg ctgggtgcct 360
ctggcgacta cgctgatttc cagtatttga agcaagttct cggccagatg gtgattgatg 420
aggagcttct gggagatgga cacagctata gtcctagagc tattcattca tggctgacca 480
gggcatgta cagccggcgc tcgaagatga accctttgtg gaacaccatg gtcacggag 540
gctatgtgta tggagagagc ttcctcgggt atgtggacat gcttggtgta gcctatgaag 600
ccccctcgt ggcactggt tatggtgcat acttggtcga gcctctgctg cgagaagttc 660
tggagaagca gccagtgcta agccagaccg agggccgcga cttagtagaa cgctgcatgc 720
gagtgtgtga ctaccgagat gcccgttctt acaaccggtt tcaaatacgcc actgtcaccg 780
aaaaaggtgt tgaaatagag ggaccattgt ctacagagac caactgggat attgccaca 840
tgatcagtgg ctttgaatga aatacagatg cattatccag aactgaagtt gccctacttt 900
taactttgaa cttggctagt tcaaagatag actcttcttt tgtaaagtaa ataaattctt 960
caaatgcaa aaaaaaaaaa aaaaaaaaaa cttcragact agttctctct c 1011

```

<210> 21

<211> 2019

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2003)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2007)

<223> n equals a,t,g, or c

<400> 21

```
ggcagagccc aattcactcc cttccctcgc agtgactttc tcattctccc tgggtacatc 60
gacttcactg cagaccaggt ggacctgact tctgctctga ccaagaaaat cactcttaag 120
accccactgg ttctctctcc catggacaca gtcacagagg ctgggatggc catagcaatg 180
gcggtgagcc ccattggggtg tgggggaagg agcaaggact ccacgcctt tcccaaagg 240
cattcagtc tgcttctkgt cacttagtag tagtctcttt ttaatcctgt agcttacagg 300
cggatttggs ttcattccacc acaactgtac amctgaattc caggccaatg aagttyggaa 360
agtgaaggty wgaagggcaa cgatcattag caagcgctcc tgggaattgc actgaggtgg 420
ggtggggtgg gagtaggggt ttattctaatt ttagtattct ttcttccac catgggggtc 480
agttactgag aagaccctga gattctgttt cttaaagcag cagcaataga ccagggtgtac 540
agtgcctcca gcctacccat gtctctaaga tgtgttggtg tgatttggtc ttgtggcact 600
gccaaaggga tcgataagca gagaccccat gcttcagatc aagagcctga tgaaagtagt 660
tcaaagatgc gatgcccttt ctaccatcc ctttccagaa atatgaacag ggattcatca 720
cagaccctgt ggtcctcagc cccaaggatc gcgtgcggga tgtttttrag gccaaaggcc 780
ggcatggttt ctgcggtatc ccaatcacag acacaggccg gatggggagc cgcttggtgg 840
gcatcatctc ctccagggac attgatttty tcaaagagga ggaacatgac tgtttcttgg 900
aagagataat gacaaagagg gaagacttgg tggtagcccc tgcaggcatc acactgaagg 960
aggcaaatga aattctgcag cgcacaagaa gggaaagtgg ccattgttaa atgaagatga 1020
tgagcttggt gccatcattg cccggacaga cctgaagaag aatcgggact acccactagc 1080
ctccaaagat gccaaagaaac agctgctgtg tggggcagcc attggcactc atgaggatga 1140
caagtatagg ctggacttgc tcgcccaggc tgggtgtggat gtagtggttt tggactcttc 1200
ccagggaagt tccatcttcc agatcaatat gatcaagtac atcaaagaca aataccctaa 1260
ctccaagtc attggaggca atgtggtcac tgcgtcccag gccaaagaacc tcattgatgc 1320
agggtgtgat gccctgcggg tgggcatggg aagtggctcc atctgcatta cgcagggaagt 1380
gctggcctgt gggcggtccc aagcaacagc agtgtacaag gtgtcagagt atgcacggcg 1440
ctttggtgtt ccggtcattg ctgatggagg aatccaaaat gtgggtcata ttgcgaaagc 1500
cttggccctt ggggtctccac agtcatgatg ggctctctcc tggctgccac cactgaggcc 1560
cctggtgaat acttcttttc cgatgggatc cggctaaaga aatatcgcg tatgggttct 1620
ctcgatgcc tggacaagca cctcagcagc cagaacagat atttcagtga agctgacaaa 1680
atcaaagtgg ccaggggagt gtctggtgct gtgcaggaca aagggtcaat ccacaaattt 1740
gtcccttacc tgattgctgg catccaacac tcatgccagg acattggtgc caagagcttg 1800
acccaagtcc gagccatgat gtactctggg gagcttaagt ttgagaagag aacgtcctca 1860
gcccagggtg aagggtggcg ccatagcctc cattcgatg agaagcggct tttctgaaaa 1920
gggatccagc acacctctc ggtttttttt tcaataaaaag tttagaaaaga aaaaaaaaaa 1980
aaaaaaaaat tctcgggggg ggnccnngta cccaattgg 2019
```

<210> 22

<211> 2022

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1588)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1615)

<223> n equals a,t,g, or c

<400> 22

```
gctttctggc gggcgctggg agaagacgga cctcacctac aggatccttc ggttcccatg 60
gcagttggtg caggagcagg tgcggcagac gatggcagag gccctaaagg tatggagcga 120
tgtgacgcca ctcaccttta ctgaggtgca cgagggccgt gctgacatca tgatcgactt 180
cgccaggtac tgcatggggg acgacctgcc gtttgatggg cctggggcat cctggcccat 240
gccttcttcc ccaagactca ccgagaaggg gatgtccact tcgactatga tgagacctgg 300
actatcgggg atgaccaggg cacagacctg ctgcaggtgg casccatgaa tttggccacg 360
tgctggggct gcagcacaca acagcagcca aggccctgat gtccgccttc tacacctttc 420
gctaccactt gagtctcagc ccagatgact gcaggggcgt tcaaacctta tatggccagc 480
cctggccact gtcacctcca ggacccagc cctgggcccc caggctggga tagacaccaa 540
tgagattgca ccgctggagc cagacgcccc gccagatgcc tgtgaggcct ccttgacgcg 600
ggtctccacc atccgaggcg agctcttttt ctccaagcg ggctttgtgt ggcgccctcg 660
tgggggccag ctgcagcccg gctaccagc attggcctct cgccactggc agggactgcc 720
cagccctgtg gacgctgcct tcgaggatgc ccagggccac atttggttct tccaagggtg 780
tcagtactgg gtgtacgacg gtgaaaagcc agtcttggg cccgcacccc tcaccgagct 840
gggcctggtg aggttcccg tccatgctgc cttggtctgg ggtcccgaga agaacaagat 900
ctacttcttc cgaggcaggg actactggcg tttccacccc agcaccggcg gtgtagacag 960
tcccgtgccc cgcaggccac tgactggaga ggggtgccct ctgagatcga cgctgccttc 1020
caggatgctg atggctatgc ctacttctg cgcgcccgcc tctactggaa gtttgaccct 1080
gtgaagggtg aggtcttggg aggttcccc cgtctctggt gtccctgactt ctttggtgtg 1140
gcgagcctgc caacactttc ctctgacctt ggcttggtat ccctcagggg tgctgacccc 1200
tgccaggcca cgaatatcag gctagagacc catggccatc tttgtggctg tgggcaccag 1260
gcatgggact gagcccatgt ctctcaggg ggatgggggt gggtagaacc accatgacaa 1320
ctgccgggag ggccacgcag gtcgtggtca cctgccagcg actgtctcag actgggcagg 1380
gaggcttttg catgacttaa gaggaagggc agtcttgggc ccgctatgca ggtcctgggc 1440
aaacctggct gccctgtctc catccctgtc cctcagggtg gcacctggc aggactggg 1500
gaactggagt gtccttgctg tatccctggt gtgaggttcc ttccaggggc tggcactgaa 1560
gcaagggtgc tggggcccca tggccttnca gccctggctg agcaactggg ctgtnagggc 1620
agggccactt cctgaggtca ggtcttggtg ggtgcctgca tctgtctgcc ttctggctga 1680
caatcctgga aatctgttct ccagaatcca ggccaaaaag ttcacagtca aatggggagg 1740
ggtattcttc atgcaggaga ccccaggccc tggaggctgc aacatacctc aatcctgtcc 1800
caggccggat cctcctgaag cccttttcgc agcactgcta tctccaaag ccattgtaaa 1860
tgtgtgtaca gtgtgtataa accttcttct tctttttttt ttttaactg aggattgtca 1920
ttaaacacag ttgttttcta aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980
aaaaaaaaaa aaaaagggcg gccgctcgcg atctagaact ag 2022
```

<210> 23

<211> 1126

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1126)

<223> n equals a,t,g, or c

<400> 23

```
cccttcccca ctgcacacac ctcagaggct gttcttgggg ccctacacct tgaggagggg 60
caggtaaaact cctgtccttt acacattcgg ctccctggag cagactctgg tcttctttgg 120
gtaaacgtgt gacgggggaa agccaaggtc tggagaagct cccaggaaca ayygatggcc 180
ttgcagcaact cacacaggac ccccttcccc taccctctcc tctctgccgc aatacaggaa 240
cccccagggg aaagatgagc ttttctaggc tacaattttc tcccaggaag ctttgatttt 300
taccgtttct tccctgtatt ttctttctct actttgagga aaccaaagta accttttgca 360
cctgctctct tgtaatgata tagccagaaa aacgtgttgc cttgaaccac ttccctcatc 420
tctcctccaa gacactgtgg acttggtcac cagctcctcc cttgttctct aagttccact 480
gagctccatg tgccctctct accatttgca gactcctgca cagttttctg gctggagcct 540
agaacaggcc tcccaagttt taggacaaac agctcagttc tagtctctct ggggccacac 600
agaaactctt tttgggctcc tttttctccc tctggatcaa agtaggcagg accatgggac 660
caggctcttg agctgagcct ctcacctgta ctcttccgaa aaatcctctt cctctgaggc 720
tggatcctag ccttaccctc tgatctccat ggcttccctc tccctcctgc cgactcctgg 780
gttgagctgt tgcctcagtc ccccaacaga tgcttttctg tctctgcctc cctcaccctg 840
agcccttcc ttgctctgca ccccatatg gtcatagccc agatcagctc ctaaccctta 900
tcaccagctg cctcttctgt gggtgacca ggtcctgtt tgctgttgat ttctttccag 960
aggggttgag cagggatcct ggtttcaatg acggttgga atagaaattt ccagagaaga 1020
gagtattggg tagatatttt ttctgaatac aaagtgatgt gtttaaatac tgcaattaaa 1080
gtgatactga aacacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaan 1126
```

<210> 24

<211> 2598

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2304)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2500)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2533)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2553)

<223> n equals a,t,g, or c

<400> 24

```
ggcacagctt gtttttccaa gcagctgttt ggctttccra agcccacttt ctgtctttaa 60
raggtttaaa garactacca gaccattttc caatgaatgt cttggtacca ccagaccctg 120
```



```

agttcctatt gattcatcag attttgcatt ggatattcgc atgcctgggg ttacacctaa 180
acagtccgat acatacttct gcatgtctat gcgaatacca gtggatgagg aagccttcgt 240
gattgacttc aagcctcgag ccagcatgga tactgtccat cacatgttac tttttggatg 300
caatatgcct tcatccactg graattactg gttttgtgat gaaggaaacct gtacagataa 360
agccaatatt ctgtatgcct gggcgagaaa tgctccccct acccggtccc ccaaagggtg 420
tggaattcaga gttggaggag agactggaag taaatacttt gtactacagg tacactatgg 480
ggatattagt gcttttagag ataataacaa ggactgttct ggtgtgtcct tacacctcac 540
acgtctgccca cagcctttaa ttgctggcat gtaccttatg atgtctgttg acactgttat 600
cccagcagga gaaaaagtgg tgaattctga catttcatgc cattrtwaaa attatccaat 660
gcatgtcttt gcctatagag ttcacactca ccatttaggt aaggtagtaa gtggatacag 720
agtaagaaat ggacagtggg cactgattgg acggcagagc cctcagctgc cacaggcttt 780
ctaccctgtg gggcatccag ttgatgtaag ttttggtgac ctactggtcg caagatgtgt 840
attcactggt gaaggaaagga cagaagccac acacattggt ggcacgtcta gtgatgaaat 900
gtgcacttat acattatgta ttacatggaa gccaaagcat cagtttcttt catgacctgt 960
accagaatg tagctccaga tatgttcaga accataccac cagaggccaa cattccaatt 1020
cccgtgaagt ctgatatggt tatgatgcat gaacatcata aagaaacaga atataaagat 1080
aagattcctt tactacagca gccaaaacga gaagaagaag aagtgttaga ccagggtgat 1140
ttctattcac tactttccaa gctgctagga gaaagggaaag atgttgttca tgtgcacaaa 1200
tataatccta cagaaaaggc agaatcagag tcagacctgg tagctgagat tgcaaatgta 1260
gtccaaaaaa aggatcttgg tcgatctgat gccagagagg gtgcagaaca tgagaggggt 1320
aatgctattc ttgtcagaga cagaattcac aaattccaca gactagtatc taccttgagg 1380
ccaccagaga gcagagtttt ctcatcacag cagccccac ctggtgaagg cacctgggaa 1440
ccagaacaca caggagattt ccacatggaa gaggcactgg attggcctgg agtatacttg 1500
ttaccaggcm aggtttctgg ggtggctcta gamcctaaga ataacctggt gattttccac 1560
agaggtgacc atgtctggga tggaaactcg ttgacagca agtttgttta ccagcaaata 1620
ggactcggac caattgaaga agacactatt ctgtgcatag atccaaataa tgctgcagta 1680
ctccagtcca gtggaaaaaa tctgttttac ttgccacatg gcttgagtat agataaagat 1740
gggaattatt gggtcacaga cgtggctctc catcaggtgt tcaaactgga tccaaacaat 1800
aaagaaggcc ctgtattaat cctgggaagg agcatgcaac caggcagtga ccagaatcac 1860
ttctgtcaac cactgatgt ggctgtggat ccaggcactg gagccattta tgtatcagat 1920
ggttactgca acagcaggat tgtgcagttt tcaccaagtg gaaagtcat cacacagtgg 1980
ggagaagagt cttcagggag cagtccctctg ccaggccagt tctactgttc tcacagcttg 2040
gctcttgtgc ctcttttggg ccaattatgt gtggcagacc gggaaaatgg tcggatccag 2100
tgttttaaaa ctgacaccaa agaatttgtg agagagatta agcatcctc atttggaaga 2160
aatgtatttg caatttcata tataccaggc ttgctctttg cagtgaatgg gaagcctcat 2220
tttggggacc aagaacctgt acaaggattt gtgatgaact tttccaatgg ggaaattatm 2280
gacatcttca agccagtgcg caancttttg gatatgcctc atgatattgt tgcacttgaa 2340
gatgggactg tgtacattgg gagatgctca taccaacacc gtgtgggaag ttccaccttg 2400
gactkgagaa awttgggaac atcggtycag tttaaaaaag ggctggscat tgaggtccag 2460
ggaaatccaa agaagcccgga gggcatttgt tgtttcccn ttacaacctc tcgggttatt 2520
ccggtggttg gtnoctggcg gggccatggc ccnaatttaa ttccggtggg aaaaaatccc 2580
aggggccctt tggaaga 2598

```

&lt;210&gt; 25

&lt;211&gt; 411

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (358)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (368)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (381)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (387)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (392)

<223> n equals a,t,g, or c

<400> 25

```
gcggccgagc tgcagcccg gctcagtcctc cgccgcccgc gtgaacatgg agcccccgga 60
cgcaccggcc caggcgcgcg gggccccgcg gctgctgttg ctgcagtcct tgctggcggc 120
gcacccagat gccacggcg aggtgcgctt gtctgtacct ccgctgggtg aggtgatgcg 180
aggaaagtct gtcattcttg actgcacccc tacgggaacc cacgaccatt atatgctgga 240
atggttcctt accgaccgct cgggagctcg cccccgccta gcctcggctg agatgcaggg 300
ctctgagctc caggtcacaa tgcacgacac ccggggccgc agtcccccat accagctnng 360
actyccangg ggcgcctggt ngctggnytg anggccark tggcgacgag.c 411
```

<210> 26

<211> 657

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (634)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (652)

<223> n equals a,t,g, or c

<400> 26

```
aactgaagaa ttttgagtga attagacctt tatttttcta tctggttgga tgggtggcttt 60
aggggaaggg ggaaaggtgt aggtggggg attgaggtgg ggaatcattt tagctggtgt 120
cagccccctc tcccttcctc cattgcacat gaacatatgt ccatccatat atattcatca 180
gaatgttaat ttattttgct ccctctgtta ggtccatttt ctaagggtag aagaggcaag 240
```

```

tggtagggat gaggtctgat aagaacccag ggtggagagg gagactcctg ggcagccgtt 300
ttcctcatcc ttccctctc ccagtcatt tccaaatgtg gcctccatgt ggggtgctagg 360
gacatgggaa aaaccactgc tatgccattt cttctctctg ttcccttcct ccccccgac 420
ggtgtggctg atgatgtctt ctggtgtcat ggtgaccacc ccctgttccc tgttctggta 480
tttcccctgt cagtttcccc tctcgccag gttgtgtccc aaaatcccct cagcctcttc 540
tctgcacgtt gctgaaggtc caggcttgcc tcaagttcca tgcttgagca ataaagtgga 600
aacaataaaa cctgggaaaa aaaaaaagg gggncgttct aaaggatccc cnagggg 657

```

&lt;210&gt; 27

&lt;211&gt; 1903

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 27

```

gggcacggga ctctgtccga ttcggcagag cacaaagttt gactccagtc tggatcgcaa 60
ggacaaattc tcctttgacc tgggaaaagg ggaggtcatc aaggcttggg acattgccat 120
agccaccatg aaggtggggg aggtgtgcca catcacctgc aaaccagaat atgcctacgg 180
ttcagcaggc agtcctccaa agattccccc caatgccacg cttgtatttg aggtggagtt 240
gtttgagttt aagggagaag atctgacgga agaggaagat ggcggaatca ttcgcagaat 300
acagactcgc ggtgaaggct atgctaagcc caatgagggt gctatcgtgg aggttgcaact 360
ggaagggtac tacaaggaca agctctttga ccagcgggag ctccgctttg agattggcga 420
gggggagaac ctggatctgc cttatggtct ggagagggcc attcagcgca tggagaaaagg 480
agaacattcc atcgtgtacc tcaagcccag ctatgctttt ggcagtggtg ggaaggaaaa 540
gttccaaatc ccaccaaattg ctgagctgaa atatgaatta cacctcaaga gttttgaaaa 600
ggccaaggag tcttgggaga tgaattcaga agagaagctg gaacagagca ccatagtga 660
agagcggggc actgtgtact tcaaggaagg taaatacaag caagctttac tacagtataa 720
gaagatcgtg tcttggctgg aatatgagtc tagtttttcc aatgagggaag cacagaaagc 780
acaggccctt cgactggcct ctcacctcaa cctggccatg tgtcatctga aactacaggc 840
cttctctgct gccattgaaa gctgtaacaa ggccttagaa ctggacagca acaacgagaa 900
gggcctcttc cgccggggag aggccacact ggccgtgaat gactttgaac tggcacgggc 960
tgatttccag aaggtcctgc agctctaccc caacaacaaa gccgccaaga cccagctggc 1020
tgtgtgccag cagcggatcc gaaggcagct tgcccgggag aagaagctct atgccaatat 1080
gtttgagagg ctggctgagg aggagaacaa ggccaaggca gaggcttcct caggagacca 1140
tcccactgac acagagatga aggaggagca gaagagcaac acggcaggga gccagtctca 1200
ggtggagaca gaagcatagc ccctctccac cagccctact cctgcggctg cctgcccccc 1260
agtctcccca ctccaccctg ttagttttgt aaaaactgaa gaattttgag tgaattagac 1320
ctttattttt ctatctgggt ggatgggtggc tttaggggaa gggggaaaagg tgtaggctgg 1380
gggattgagg tggggaatca ttttagctgg tgtcagcccc tcttcccttc ctccattgca 1440
catgaacata tgtccatcca tatatattca tcagaatgtt aatttatttt gctccctctg 1500
ttaggtccat tttctaagg tagaaggagc aagtggtagg gatgaggtct gataagaacc 1560
cagggtggag agggagactc ctgggcagcc gttttcctca tcctttccct ctcccagtc 1620
atttccaaat gtggcctcca tgtgggtgct agggacatgg gaaaaaccac tgctatgcca 1680
tttcttctct ctgttccctt cctcaccctg acgtgtggcc ctaaggctgt gccacctccc 1740
cctgccagct ccctggtctc tgtacagtgt ctgtccagga cgtctatcca tccatccttg 1800
acaacctgtc cagatgaggc cactgttatc ccagtctgtg aggggcatc acagcccagg 1860
tgccggccga tgtggagacg ctgatggact tcagtgtgca gga 1903

```

&lt;210&gt; 28

&lt;211&gt; 1333

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<220>  
<221> misc feature  
<222> (1311)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1313)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1319)  
<223> n equals a,t,g, or c

<400> 28  
ggccgctagt gccagctcg cagaaggcgc tgctgctgga gctcaagggg ctgcaggaag 60  
agccggtcga gggattccgc gtgacactgg tggacgaggg cgatctatac aactgggagg 120  
tggccatctt cgggcccccc aacacctact acgagggcgg ctacttcaag gcgcgcctca 180  
agttcccat cgactacca tactctccac cagccttctg gttcctgacc aagatgtggc 240  
accctaacat ctacgagacg ggggacgtgt gtatctccat cctccaccg ccggtggacg 300  
acccccagag cggggagctg ccctcagaga ggtggaaccc cacgcagaac gtcaggacca 360  
ttctctgag tgtgatctcc ctctgaacg agcccaacac cttctcgccc gcaaactgg 420  
acgctccgt gatgtacagg aagtggaaag agagcaaggg gaaggatcgg gagtacacag 480  
acatcatccg gaagcaggtc ctggggacaa ggtggacgcg ggtgaacggc gtgaagggtc 540  
ccaccacgt gcccgagtac tgcgtgaaga ccaaggcgcc gccgcccac gaggggttcag 600  
acctcttcta cgacgactac tacgaggacg gcgaggtgga ggaggaggcc gacagctgct 660  
tcggggacga tgaggatgac tctggcacgg aggagtcttg acaccaccag aataaacttg 720  
ccgagtttac ctactaggg ccggaccctg ggctccttag acgacagact acctcacgga 780  
ggttttgtgc tgggtccctg ctctctggt tgtttcgttt tggctttttc tccctcccca 840  
tgtctgttct gggttttcac gtgcttcaga gaagaggggc tgccccaccg ccactcacgt 900  
cactcggggc tcggtggacg ggcccagggt gggagckgcc ggcccacctg tcccctcggg 960  
aggggagctg agcccactt ctaccggggt cccccagctt ccggactggc cgcaccccg 1020  
aggagccacg ggggcgctgc tgggaacgtg ggcggggggc cgtttctga cactaccagc 1080  
ctgggaggcc cagggtgtagc ggtccgaggg gcccggtcct gcctgtcagc tccaggtcct 1140  
ggagccacgt ccagcacaga gtggacggat tcaccgtggc cgactctttt ccctgctttg 1200  
gtttgtttga aatctaaata aaactacttt atgagaaaaa aaaaaaaaaa aaaaaaaaaa 1260  
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa nanaaaaaana 1320  
aaaaaaaaaa ttt 1333

<210> 29  
<211> 1327  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (573)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1307)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1325)  
<223> n equals a,t,g, or c

<400> 29  
cttggttctcc gccgccgccg cccgccgccg ccgccrccgc cgcygccgct gccatggctc 60  
aatacaaggc cgccgcgagc gaggccggcc gcgccatgca cctgatgaag aagcgggaga 120  
agcagcgcca gcagatggag cagatgaagc agcgcacgcs ggaggagAAC atcatgaaat 180  
ccaacattga caagaagttc tctgcgcact acgacgcggt ggaggcagag ctcaagtcca 240  
gcaccgtggg tctcgtgacc ctgaatgaca tgaaggccaa gcaggaggct ctggtgaagg 300  
agcgggagaa gcagctggcc aagaaggagc agtccaagga gctgcagatg aagctggaga 360  
agcttcgaga gaaggagcgt aagaaggaa ccaagcgaa gatctccagc ctgtccttca 420  
ccctggagga ggaagaagag ggaggcgagg aggaagagga ggcggccatg tatgaggagg 480  
agatggaaag ggaagagatc accacgaaga agagaaaact ggggaagaac ccagacgttg 540  
acacaagctt cttgcctgat cgagaccgtg agnaggagga gaatcggctt cgggaagagc 600  
tgccggcagga gtgggaagcc aagcaggaga agatcaagag tgaggagatc gagatcacct 660  
tcagctactg ggatggctct gggcaccggc ggacagtcaa gatgagaaag ggcaacacca 720  
tgcagcagtt cctgcagaag gcgctcgaga tccttcgaa agacttcagt gagctgaggt 780  
ccgcagggkt ggagcagctc atgtacatca aggaggactt gatcatccct caccatcaca 840  
gcttctacga cttcatcgtc accaaggcac gggggaagag tggaccactc ttcaactttg 900  
atgttcatga cgatgtgcgg ttgctcagtg acgccactgt ggagaaggat gagtcccatg 960  
caggcaagggt ggtgctgagg agctggtagc agaagaacaa gcacatcttt cccgccagcc 1020  
gctgggaacc ctacgacctt gaaaagaagt gggacaagta cacgatccgc tgagcatcca 1080  
ggaggctgcg cggccccggc tcctcagctc cctcagtgtg ccccggtgtg tcaccgggac 1140  
tccaggcacc cgctcccctg cgaccatgcc aggcacgctg ggaggaggac ggcagctgct 1200  
cgtgtcctgc cctgccaca tcagtgactg ctttattctt ttccaataaa gaagtgcacg 1260  
tgtcagagct ggagcgctg cattgtgaga aaaaaaaaaa gaggggnaag aaaaaaaaaa 1320  
agggngg 1327

<210> 30  
<211> 709  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (696)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (701)  
<223> n equals a,t,g, or c

<400> 30

```

aattcccggg ttcgaccac gcgtccggaa aactgcagct tccttctcac cttgaagaat 60
aatcctagaa aactcacaaa atgtgtgatg cttttgtagg tacctggaaa cttgtctcca 120
gtgaaaactt tgatgattat atgaaagaag taggagtggg ctttgccacc aggaaagtgg 180
ctggcatggc caaacctaac atgatcatca gtgtgaatgg ggatgtgatc accattaaat 240
ctgaaagtac ctttaaaaaat actgagattt ccttcatact gggccaggaa tttgacgaag 300
cactgcagat gacaggaaaag tcaagagcac cataacctta gatgggggtg tcctgggtaca 360
tgtgcagaaa tgggatggaa aatcaaccac cataaagaga aaacgagagg atgataaact 420
gggtggggaa tgcgtcatga aaggcgtcac ttccacgaga gtttatgaga gagcataagc 480
caagggacgt tgacctggac tgaagtccgc attgaactct acaacattct gtgggatata 540
ttgttcaaaa agatattgtt gttttccatg atttagcaag caactaattt tctcccaagc 600
tgattttatt caatatgggt acgttggtta aataaacttt ttttagattt aaaaaaaaaa 660
aaaaaaaaacc ycgggggggg gcccgggtacc caattngccc nttaggggg 709

```

<210> 31

<211> 1108

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (389)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (397)

<223> n equals a,t,g, or c

<400> 31

```

tgcttatcct tgtgctgatg tttgtggtat ggatgaaacg ccgggataaa gaacgccagg 60
ccaaacaact tttaattgat ccagaagatg atgtaagaga taatatattt aaatatgatg 120
aagaaggtgg aggagaagaa gaccaggact atgacttgag ccagctgcag cagcctgaca 180
ctgtggagcc tgatgccatc aagcctgtgg gaatcygacg aatggatgaa agacctatcc 240
acgccgagcc ccagtatccg gtccgatctg cagccccaca ccctggagac attggggact 300
tcattaatga gggccttaaa gcggctgaca atgacccac agctccacca tatgactccc 360
tgtagtggtt tgactatgaa ggcagtggnt cactgntgg gtccttgagc tcccttaatt 420
cctcaagtag tgggtggtgag caggactatg attacctgaa cgactggggg ccacggttca 480
agaaacttgc tgacatgtat ggtggagggtg atgactgaac ttcagggtga acttggtttt 540
tggacaagta caaacaattt caactgatat tcccaaaaag cattcagaag ctaggcttta 600
actttgtagt ctactagcac agtgcttgct ggaggctttg gcataggctg caaaccaatt 660
tgggctcaga gggaatatca gtgatccata ctgtttggaa aaacactgag ctgagttaca 720
cttgaatttt acagtacaga agcactggga ttttatgtgc ctttttgtag ctttttcaga 780
ttggaattag ttttctgttt aaggctttaa tggtagtgat ttctgaaacg ataagtaaaa 840
gacaaaatat tttgtggtgg gagcagtaag ttaaaccatg atatgcttca acacgctttt 900
gttacattgc atttgctttt attaaaatac aaaattaaac aaamaaaaaa actcatggag 960
cgattttatt atcttggggg atgagacat gagattggaa aatgtacatt acttctagtt 1020
ttagacttta gtttggtttt tttttttttt cactaaaatc ttaaaactta ctgagctggt 1080
tgcaataaaa gggagttttc atatcacc

```

1108

<210> 32

<211> 526

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (502)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (524)

<223> n equals a,t,g, or c

<400> 32

```
gaatttttca ttatgttgct tttgaaattt gatgcattcc tcccatttac tttattattg 60
tacacattta acacacagta gcaaattttg aacgatgtga ttgatataac ctaacaaatc 120
tgagccagtt attattagag ttgcagaata gaaacttgaa gtgctaaatg gaataatcca 180
aaggaaaattt tttaaatgca ggttctagct gaaaaattca actataagaa aattgtattt 240
atataacatt tactattttt gaagactagt gagatttctg taataatttt aattcctttaa 300
aaagtgaag cttgttgtaa agatattttc tttttgttat tagaaggaaa tacaagagaga 360
aaaatttctt tctttcatgg ggcatttgat aatttcagtc tttgacgatt tgtaagccta 420
gaatatacta agctgaataa cagctctttg gcctcagaat tttccagtag ccagtawttc 480
yggattaact aagttggaaa cncytattag gaacctccag tggnga 526
```

<210> 33

<211> 555

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (494)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (521)

<223> n equals a,t,g, or c

<400> 33

```
ccggaccctg caccagcga ctgggccccg cgcgcgccct ccgcgagggg ggaggcggcg 60
gctgtgtgcg cagggcccg caccggactg ggaccctggc gtccctccag gccttgctc 120
ctgcgggags acagtttggc ttactttctc tgacccagc ctcggccgta aagtgaaga 180
gaccggacca gcttcagctt tcggactctg gttcttgat cgtgtcctct cccctcgcg 240
gccctcttcc cccaatctga gccattkcag gcctctgcct gckgccccct ctctcctcgg 300
gatcgggtcc ccagagccac catctcctga gcctcccacc ccgctgcctg ggccctgtgg 360
ttgctgggccc tcccacctca aggaggggaa ggttgtacag cccgaaccgg tggagcaatg 420
ccctgtctgg cctccaaaac caaaataaaa ctgggtcact ttacaaaaaa aaaaaaaaaa 480
aaggggccccg gaanaccgga ccggtacctg caggcgtacc ngtttcccta tagtgagttg 540
tattagcgtt gcata 555
```

<210> 34  
 <211> 347  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (288)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (328)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (335)  
 <223> n equals a,t,g, or c

<400> 34  
 gggctcgaccc acgcgtccgg accgcgcggc tagtggtgtg aggatctgag ccccggtggtg 60  
 gggggtggag gcggctcctg cratctaaag ggacttgaga ctctcaccgg ccgcgcgcca 120  
 tgagggccct gtgggtgctg ggcctctcct gcrtcctgct gaccttcggg tcggtccgar 180  
 ctgaygatga agtcgatgtg gatggtacag tggaagagga tctgggtaaa agtagagaag 240  
 gttcaaggac agatgatgaa gtagtacaga gagaggaaga agctattnca gttggatgga 300  
 ttaaattgcat cccaaataag agaacttnag agagnaagtc cagaaaa 347

<210> 35  
 <211> 750  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (701)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (731)  
 <223> n equals a,t,g, or c

<400> 35  
 ggggtggcttc cttgtggttc ctcatgtgtg cctgcaaccc ctggttcacc tccttccagg 60  
 ttctgggtcc ttccagccat ggctctcaga gtccttctgt taacagcctt gaccttatgt 120  
 catgggttca acttggacac tgaaaacgca atgaccttcc aagagaacgc aaggggcttc 180  
 gggcagagcg tgggtccagct tcagggatcc aggggtggtg ttggagcccc ccaggagata 240  
 gtggctgcca accaaaaggg cagcctctac cagtgcgact acagcacagg ctcatgagag 300  
 cccatccacc tgcaggtccc cgtggaggcc gtgaacatgt ccctgggcct gtccctggca 360  
 gccaccacca gccccctca gctgctggcc tgtggtccca ccgtgcacca gacttgcagt 420



gagaacacgt atgtgaaagg gctctgcttc ctgtttggat ccaacctacg gcagcagccc 480  
cagaagttcc cagaggccct ccgaggggtgt cctcaagarg atagtgcacat tgccttcttg 540  
attgatggct ctggtagcat catccacat gactttcggc ggatgaagga rtttgtctca 600  
actgtgatgg agcaattaaa aaagtccaaa accttgttct ctttgatgca gtactctgaa 660  
gaattccgga ttcactttac ttcaaagagt tccagaacaa ncctaaccga agatcactgg 720  
tgaagccaat nacgcagctg cttggggcgg 750

<210> 36

<211> 1291

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (29)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (298)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (695)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (795)

<223> n equals a,t,g, or c

<400> 36

aagaaaaatg tactacgcct gtcctgtang aagctgaaga tttttgcaat gcccatgcag 60  
gatatcaaga tgatcctgaa aatggtgcag ctggactcta ttgaagattt gggaagtgcac 120  
ttgtacctgg aagctaccca ccttggcgaa attttctcct tacctggggc agatgattaa 180  
tctgcgtaga ctctcctct cccacatcca tgcattctcc tacatttccc cggagaagga 240  
agagcagtat atcgcccagt tcacctctca gttcctcagt ctgcagtgcc tgcagctnct 300  
ctatgtggac tctttatttt tccttagagg ccgcctggat cagttgctca ggcacgtgat 360  
gaaccoccttg gaaaccctct caataactaa ctgccggcct tcggaagggg atgtgatgca 420  
tctgtcccag agtcccagcg tcagtcagct aagtgctctg agtctaagtg gggtcagtgc 480  
gaccgatgta agtcccagc ccctccaagc tctgctggag agagcctctg ccaccctcca 540  
ggacctggtc tttgatgagt gtgggatcac ggatgatcag ctcttgccc tcctgccttc 600  
cctgagccac tgctcccagc ttacaacctt aagcttctac gggaattcca tctccatata 660  
tgccttgcaag agtctcctgc agcacctcat cggngtgagc aatctgacct acgtgctgta 720  
tcctgtcccc ctggagagtt atgaggacat ccatgggtamc ctccamctgg agagggtgct 780  
atctgcatgc caggntcagg gagttgctgt gtgarttggg gcggcccagc atggttcttg 840  
cttagtgggc aaccctgtc ctcactgtgg ggacagaacc ttctatgacc cggagcccat 900  
cctgtgcccc tgtttcatgc ctaatarctg ggtgcacata tcaaagtctt cattctgcat 960  
acttgacac taaagccagg atgtgcatgc atcttgaaagc aacaaagcag ccacagtttc 1020  
agacaaatgt tcagtgtgag tgaggaaaac atgttcagtg aggaaaaaac attcagacaa 1080

atgttcagtg agggaaaaaa ggggagttgg ggataggcag atgttgactt grggagktaa 1140  
tgtgatcttt ggggagatac atcttataga gttagaaata gaatctgaat ttctaaaggg 1200  
agawtctggc ttgggaagta catgtaggag ttaatccctg ttagactgt tgtaaagaaa 1260  
ctgttgaaaa taaagagaag caatgtgaag c 1291

<210> 37  
<211> 1535  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1413)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1526)  
<223> n equals a,t,g, or c

<400> 37  
ggcacgaggg tacgcagagc ttcgtcttcc agcgcgaaga gatagcgagc ttggcgcggc 60  
agtacgctgg gctggaccac gagctggcct tctctcgtct gatcgtggag ctgcggcggc 120  
tgcacccagg ccacgtgctg cccgacgagg agctgcagtg ggtgttcgtg aatgcgggtg 180  
gctggatggg cgccatgtgc cttctgcacg cctcgtctgc cgagtatgtg ctgctcttcg 240  
gcaccgcctt gggctcccgc ggccactcgg ggcgctactg ggctgagatc tcggatacca 300  
tcctctctgg caccttccac cagtggagag agggcaccac caaaagtga gtcttctacc 360  
caggggagac ggtagtacac gggcctggtg aggaacacgc tgtggagtgg gggccaaaca 420  
catggatggt ggagtacggc cggggcgctc tcccatccac cctggccttc gcgctggccg 480  
acactgtctt cagcaccag gacttcctca ccctcttcta tactcttcgc tctatgctc 540  
ggggcctccg gcttgagctc accacctacc tcttgggcca ggacccttga ccagccaggc 600  
ctgaaggaag acctgcggat ggacaggagc gggcaggccc gcacatatcc acttgctgga 660  
gcccattgtt acagacaggg acatacacca tgcagatcct gatttcctgc tgtatgagca 720  
gggatatacca tgcttatgta tccaaacaca gagacccatg ggaacaaatg agacacatat 780  
agatactgag acctgtgtgt acagtaggac catgcactca caccatctg gagaggagc 840  
ccccggtata ccaaggagc cagttgtgtt cagacacaca catcacagct tgactcacta 900  
actgaggcct ttccatagct ccacagcttc ccacctcctc cccaccaaac cggggttcta 960  
gagttaagga tgggggaggg tattatactg cctcagctctg actcctcaac ccagcagcaa 1020  
tttgagggga tgaggggaa gaggagctgc cttttggagg ccccttcac ctgcagctat 1080  
gatgcccttc cccttctccc ctgtcctcac catatgcctt atccccattc tactccctg 1140  
ctatgcaagt gcccctgtgg cttgtcccca accccctcag caacaaagct cagctgggga 1200  
acgagagtaa tttgaagaat gcttgaagtc agcgtcttcc attccagaaa gaccccat 1260  
cttccttttg gggatatgat tggaagctgg ttccagccca ggaccacca ctgaggagag 1320  
gatctagaca ggtgggccta attccaaggg gcccttcctg gcctggagaa ggccttttac 1380  
acacacacaa cacatacaca cacacacaca canacacata tcacagttt cacacagccc 1440  
ctgctgcatt ctctgtccat ctgtctgtt ctattaataa agatttggtg atctgttcca 1500  
aaaaaaaaa aaaaaaaaaa aaaaangggg gggtc 1535

<210> 38  
<211> 295  
<212> DNA

<213> Homo sapiens

<400> 38

```
ctggtcacac tattacatgc catgcaggca cgcgataaaa cgctggggct ggcaacactg 60
tgcattggcg gcggtcaggg aattgcgatg gtgattgaac ggttgaatta atcaataaaa 120
acacccgata gcgaaagtta tcgggtgttt tcttgaacat cgacggcgaa ggtaacccca 180
ttaatcacca gtcaaaaactt ttcaccagcg tcaactcgcca gcattacgca tcggtacaat 240
aaatgtttcc tgtttctcat tgaccgatcc ttcacggtg atcagcgtca ttggg 295
```

<210> 39

<211> 1300

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (641)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1297)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1298)

<223> n equals a,t,g, or c

<400> 39

```
gcggaactggc agggggcagg gaagctcaaa gatctgggggt gctgccagga aaaagcaaatt 60
tctggaagtt aatgggtttt agtgattttt aaatccttgc tggcgagag gcccgcctct 120
ccccggtatc agcgcttccct cattctttga atccgcggct ccgcggtctt cggcgctcaga 180
ccagccggag gaagcctggt tgcaatttaa gcgggctgtg aacgcccagg gccggcgagg 240
gcggggccga ggcgggccat tttraataaa gaggcgtgcc ttccaggcag gctctataag 300
traccgccc ggcgagcgtg cgcgckttgc aggtcactgt agcgggactt cttttggttt 360
tctttctctt tggggcacct ctggactcac tccccagcat gaaggcgtg agcccgggtg 420
gcggctgcta cgaggcgggtg tgctgcctgt cggaacgcag tctggccatc gcccggggcc 480
gagggaaagg cccggcagct gaggagccgc tgagcttgct ggacgacatg aaccactgct 540
actcccgcct gcggraactg gtacccggag tcccagagg cactcagctt agccagggtg 600
aaatcctaca gcgcgtcatc gactacattc tcgacctgca ngtagtcctg gccgagccag 660
cccctggacc ccctgatggc cccacacctc ccatccagac agccgagctc gctccggaac 720
ttgtcatctc caacgacaaa aggagctttt gccactgact cggccgtgtc ctgacacctc 780
cagaacgcag gtgctggcgc ccgttctgcc tgggacccc ggaacctctc ctgccggaag 840
ccggacggca gggatgggcc ccaacttcgc cctgccact tgacttcacc aaatccctc 900
ctggagacta aacctggtgc tcaggagcga aggactgtga acttggtggc tgaagagcca 960
gagctagctc tgccaccag ctgggcgagc tcacctgct cccacccac cccaagttc 1020
taaggctcty tcagagcgtg gaggtgtgga aggagtggct gctctccaaa ctatgccaa 1080
gcggcgccag agctggctct ctggtctcct tggagaaagg ttctgttgcc ctgatttatg 1140
aactctataa tagagtatat aggttttcta ctttttttac aggaaggtga ctttctgtaa 1200
caatgcgatg tatattaaac tttttataaa agttaacatt ttgcataata aacgattttt 1260
```

aaacaaaaaa aaaaaaaaaa aagggggggcc gccctanngg

1300

<210> 40

<211> 215

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (210)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (213)

<223> n equals a,t,g, or c

<400> 40

cagaaacaga agttcacact aacagagtat ggttttaatt ttcctttgaa tgaaaaggat 60  
 agaaagataa aattgtgtat tgtaacatg taaataaaat tggagctaata ttgaaactag 120  
 cttctcaata acttcacatt tctagagact cattacctgt gggcttgctm aacctggact 180  
 atttggccaa atwgggttga taaaaaaggn atntt 215

<210> 41

<211> 474

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (85)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (216)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (374)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (449)

<223> n equals a,t,g, or c

<400> 41

tcgacccacg cgtccgggag actacggtaa aggcgcgcgc acgcagccaa catgccggtg 60  
 gcccgagct gggtttgcg caagnctacg tgaccctcg gaggccctt gagaagtcg 120

```

ggctcgacca agagctgaag ctgataggcg agtacgggct ccggaacaaa cgtgaggtgt 180
ggaggggtcaa gttcacccctg gccaaagatcc gcaagnccgc gcgggarctg ctgacgctgg 240
acgagaagga cccgcggcgc ctgtttgagg gcaatgcctt gcttcggcga ctggtgcgca 300
ttggagtgtc ggacgagggc aagatgaagc tggattatat cctgggtctg aagatgagga 360
ttcttgga grontctgca gaccaggtt tttcaagctg gggttgcca atccatccac 420
catgccctgt gctgatccgc caggccacnc aggtccgaaa gcaagtgtg aaca 474

```

<210> 42

<211> 425

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (375)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (403)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (418)

<223> n equals a,t,g, or c

<400> 42

```

cctcgcccttc gatgaatatg ggcgcccttt cctcatcatc aaggatcagg atcgcaagtc 60
tcgtcttatg ggactggagc tctcaagtct catatcatgg cggcaaaggc ttagcaaat 120
accatgagaa catcacttgg accaaatgga cttgataaaa tgatggtgga caaggacggc 180
gacgtgacgg tcacaaacga cgtgccacg attctgagca tgatggatgt cgatcaccag 240
attgccaaagc tgatggtgga gctgtccaaa tcccaggatg atgaaatcgg agatggggac 300
cacgggggtg gttgtcctgg ccggcgccct gctggaagga ggccgagcag ctgctggacc 360
gcggcattca mccgntcagg atcgccgacg gttacgagca ggntgcccgc attggccntc 420
gagca 425

```

<210> 43

<211> 1187

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (33)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (41)

<223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1149)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1156)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1160)  
 <223> n equals a,t,g, or c

<400> 43  
 tgtgggaact ggtgggtccc ccgggctggc agnaattggg nacgcgggtc gcggttcttg 60  
 tttgtggatc gctgtgatcg tcaattgaca atgcagatct tcgtgaagac tctgactggt 120  
 aagaccatca ccctcgaggt tgagcccagt gacaccatcg agaattgtcaa ggcaaagatc 180  
 caagataagg aaggcatccc tcctgaccag cagaggctga tctttgctgg aaaacagctg 240  
 gaagatggkc gcaccctgtc tgactacaac atccagaaaag agtccaccyt gcacctggtr 300  
 ctccgtctca gaggtgggat gcaaatcttc gtgaagacac tcaactggcaa gaccatcacc 360  
 cttgaggtcg agcccagtga cacyatcgag aacgtcaaag caaagatcca rgacaaggaa 420  
 ggcattcctc ctgaccagca gaggttgatc tttgccggaa agcagctgga agatgggctg 480  
 accctgtctg actacaacat ccagaaagag tctaccctgc acctggtgct ccgtctcaga 540  
 ggtgggatgc agatcttcgt gaagaccctg actggtaaga ccatcacyst cgargtggag 600  
 ccgagtga caattgagaa tgtcaaggca aagatccaag acaaggaagg catccctcct 660  
 gaccagcaga ggttgatctt tgctgggaaa cagctggaag atggacgcac cctgtctgac 720  
 tacaacatcc agaaagagtc caccctgcac ctggtgctcc gtcttagagg tgggatgcag 780  
 atcttcgtga agaccctgac tggtaagacc atcaactctc aagtggagcc gactgacacc 840  
 attgagaatg tcaaggcaaa gatccaagac aaggaaggca tccctcctga ccagcagagg 900  
 ttgatctttg ctgggaaaca gctggaagat ggacgcaccc tgtctgacta caacatccag 960  
 aaagagtcca ccctgcacct ggtgctccgt ctyagagggt ggatgcagat cttcgtgaag 1020  
 accctgactg gtaagaccat cacyctcgaa gtggagccga gtgacaccat ygagaatgtc 1080  
 aaggcaagat ccagacaagg aaggcatcct cctgaccagc agargttgat tttgctggga 1140  
 aaarcttgna aatggncgan cccttttgat taaaatcccc aaagtcc 1187

<210> 44  
 <211> 515  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (217)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (465)

<223> n equals a,t,g, or c

<400> 44

```
ctgcagtacc gtccgaattc ccgggtcgac ccacgcgtcc ggtttgagcc gtcgtgcttc 60
accggtctac ctgcctagca tgtcgggccg cggcaagact ggccggcaagg cccgcgcca 120
ggccaagtgc cgtcgtcgc gcgcggcct ccagttccca gtgggcccgtg tacaccggt 180
gctgcggaag ggccactacg ccgagcgcgt tggcgcnngc rcgccagtgt acctggcggc 240
agtgtggag tacctcaccg ctgagatcct ggagctggcg ggcaatgcgg cccgcgacaa 300
caagaagacg cgaatcatcc cccgccacct gcagctggcc atccgcaacg acgaggagct 360
caacaagctg ctgggcggcg tgacgatcgc ccagggaagg cgtctgccc aacatccagg 420
ccgtggttg tgcccaagaa gaccagcgc accgtggggc cgaangccct tcggggggca 480
agaaagggca accaaggctt cccaaggagt actaa 515
```

<210> 45

<211> 1499

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1476)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1492)

<223> n equals a,t,g, or c

<400> 45

```
gcgagtgcgc gctcctcctc gcccgccgct aggtccatcc cggcccagcc accatgtcca 60
tccattcag ctccccggca tccgcgaggt caccattaac cagagcctgc tggccccgct 120
gcggtggac gccgaccctt cctccagcg ggtgcgccag gaggagagcg agcagatcaa 180
gacctcaac aacaagtttg cctcctcat cgacaagggt cggtttcttg agcagcagaa 240
caagctgctg gagaccaagt ggagctgct gcaggagcag aagtcggcca agagcagccg 300
cctcccagac atctttgagg ccagattgc tggccttcgg ggtcagcttg aggcactgca 360
ggtggatggg ggccgcctgg aggcggagct gcggagcatg caggatgtgg tggaggactt 420
caagaataag tacgaagatg aaattaaccg ccgcacagct gctgagaatg agtttgtggt 480
gctgaagaag gatgtggatg ctgcctacat gagcaagggt gagctggagg ccaagggtga 540
tgccctgaat gatgagatca acttcctcag gacctcaat gagacggagt tgacagagct 600
gcagtcccag atctccgaca catctgtggt gctgtccatg gacaacagtc gctccctgga 660
cctggacggc atcatcgctg aggtcaaggc rcagtatgag gagatggcca aatgcagccg 720
ggctgaggct gaagcctggt accagaccaa gtttgagacc ctccaggccc aggctgggaa 780
gcatggggac gacctccgga ataccggaa tgagatttca gagatgaacc gggccatcca 840
gaggctgcag gctgagatcg acaacatcaa gaaccagcgt gccaaagtgg aggccgccat 900
tgccgaggct gaggagcgtg gggagctggc gctcaaggat gctcgtgcca agcaggagga 960
gctggaagcc gcctgcagc gggccaagca ggatatggca cggcagctgc gtgagtacca 1020
ggaactcatg agcgtgaagc tggccctgga catcgagatc gccacctacc gcaagctgct 1080
ggagggcgag gagagccggt tggctggaga tggagtggga gccgtgaata tctctgtgat 1140
gaattccact ggtggcagta gcagtggcg tggcattggg ctgacctcg ggggaacat 1200
gggcagcaat gccctgagct tctccagcag tgcgggtcct gggctcctga aggtttatc 1260
catccggacc gcatccgcca gtcgcaggag tgcccgcgac tgagccgcct cccaccactc 1320
```

cactcctcca gccaccaccc acaatcacaa gaagattccc acccctgcct cccatgcctg 1380  
 gtoccaaagac agtgagacag tctggaaagt gatgtcagaa tagcttccaa taaagcagcs 1440  
 tcattctgag gcctgagtga aaaaaaaaaa aaaaanaaaa aaaaaaattt tngggggggg 1499

<210> 46  
 <211> 393  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (167)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (178)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (219)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (359)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (372)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (378)  
 <223> n equals a,t,g, or c

<400> 46  
 tcgacccacg cgtccggcag cctttctgag ggagcggttg tgtgttcgcc atcttaggaa 60  
 gaagatgttc tcgtccgtgg cgcattctggc cgggcgaaacc ccttcaacgc gccccacctg 120  
 cagctggtag acgatggcct cacgggcacc gaagcagccc cgtgggnacc cccgggcncg 180  
 ccccgaaagt tcccgaatc tggcagcagc cgctgtggna agagtacagt tgccaatatg 240  
 gctccatgaa gttttatgca ctgtgtggct ttgggtgggt cttagttgt ggtctgacac 300  
 aactgtctgt cgttctctg gatttagtga aatgccgaat gcargtggac cccagaant 360  
 acaaggcack wnttaatngg attctcatta aca 393

<210> 47  
 <211> 238  
 <212> DNA



<213> Homo sapiens

<400> 47

```
cggatcccg ctcctgcac cagtcgccat tcgggaggcc gctgcgctgc agggcctcgc 60
ggaccgccc cgaccgcgag ccgggcccctc cgcgcggtcc atcgcccact ggacgcccgc 120
cgcggccgga ccggttcaac ttctcatctt tgttcttctt catatactat aggtgtttg 180
ctgtggttta gtcaaaaagc catgtagaat gcctgccttt tgaagaccac ttttaagg 238
```

<210> 48

<211> 939

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (937)

<223> n equals a,t,g, or c

<400> 48

```
gccaccatct tggaacggga ggcggagcag agtcgactgg gagcgaccga gcgggcccgc 60
gccgcccga tgaaccccga atatgactac ctgtttaagc tgcttttgat tggcgactca 120
ggcgtgggca agtcatgcct gtcctgcgg tttgctgatg acacgtacac agagagctac 180
atcagacca tcggggtgga cttcaagatc cgaaccatcg agctggatgg caaaactatc 240
aaacttcaga tctgggacac agcgggccag gaacggttcc ggaccatcac ttccagctac 300
taccgggggg ctcattggcat catcgtggtg tatgacgtca ctgaccagga atcctacgcc 360
aacgtgaagc agtggctgca ggagattgac cgctatgccg gcgagaacgt caataagctc 420
ctggtgggca acaagagcga cctcaccacc aagaagggtg tggacaacac cacagccaag 480
gagtttgtag actctctggg catccccttc ttggagacga gcgccaagaa tgccaccaat 540
gtcagagcag cgttcatgac catggctgct gaaatcaaaa agcggatggg gcctggagca 600
gcctctgggg gcgagcggcc caatctcaag atcgacagca cccctgtaa gccggtggc 660
ggtggctgtt gctagsagg gcacatggag tgggacagga gggggcacct tctccagatg 720
atgtccctgg agggggcagg aggtacctcc ctctccctct cctggggcat ttgagtctgt 780
ggctttgggg tgctctgggc tccccatctc ctctcgccc atctgcctgc tgccctgagc 840
cccggttctk tmaggtccc taaaggagga cactcagggc ctgtggcagg caggggcgag 900
gctgcttggt ctgttgctc taagtgaatt tccaaangc 939
```

<210> 49

<211> 1771

<212> DNA

<213> Homo sapiens

<400> 49

```
tctgaggctc ctggggagtc ggtgggaacg acaccagaag ctcagatgaa gactggccca 60
tttgagagc actccaacca gctgtggaac atcagcgcg tcccttctct gtccaaagt 120
aaccagggtc tcatccgcat gtataaggcc gagtgcctgg agaagtccc tgtgatccag 180
cacttcaagt tcgggagcct gctgccatc catcctgtca cgtcgggcta ggaggggcca 240
agccgaagag ccaccaggc cacagttcct gtgcctgcct tccccacccc agcagtggc 300
cctccccatc cctccctct gtctgtccg tttgatgaga ggctgtttac tggggtggg 360
tggcgagatg ggcttgagg ggctcagagc ataaggcttc agggcccaag ttgggagaag 420
tgaccaaagt gtagccagtt ttctgagtt ccgtgtgcta gactggccag aagagagggt 480
ctggggcctg gtcactcggc cactctctcc tgtttctggc ctcttctccc ttcactccc 540
```

```

tccagtctgg ttttgagagc aggggctgtt ctgcagcacc kcagggaagg gaggagagat 600
acctgctgct tccattgctt ttcccttcct ggagtcgatg cctttctaag ggttgagact 660
gctccttgca ggggcgggtc agtttcccag gccatgccgg ggtggccatc tatgctaggg 720
ctggaagctg aggttgccg ccagctgtgg gctgggggtg ggtgggtggg gtcgggtggg 780
ggagaggcct tagctgtcct ggctggtgcc cctcccaggc tccttttcac cctgccccct 840
gggcctgagg cccctgtgt ccaagcctcc ccctggctct tcagttctct agcccttggc 900
tttgctgggt ttctgactg tagccacatc tctcccgtc cctaagggtg acctagccaa 960
tggaagctgc ctttgggta ggtgctgggc tcctgggagg gccagatga tggggtgagg 1020
catgtctttc cagaactttc cctggcaggg aggggatggc agaaactcag ggaggggctt 1080
ggggccatt gtatctggag agcctggatt cctcttgga gtcttaggcc crgccacttc 1140
tgctaccttt gcgtgctgt gagcctcacc ctggggccct gggccctgct tctctgtctc 1200
cctgggtgat gggcgggcc agaaggtggc agtcccacac cttgtcctcc cactccctg 1260
aactgtccat tgcttttata ggggtgaggta agwgacagcc tcccaagccc aggcttggc 1320
actcagaatg tgcccagtg gggctgggca ggcccattga ggccaccgc cgaggtttct 1380
cctagggtctg ttctgggcc tggctcttac aggtcgtcc cccaggcctg cccttctcca 1440
ctgccccctc ctgtgtctg gtccacacac ccttcaggaa gggggagcac tgagaagcac 1500
agcacagggg ctgacctg gatccgtga tggctctggc agaggctggg tcaggagtcc 1560
caaaggctcag tgacagtttc tcagaagagg ccagcgtcc acctctctcc cagggccaga 1620
cacccttcc tggtcccc atccccctat ggctcccagc cccttgacc ctcatgtctg 1680
ttcagattaa agcctctgtt ttgcacctgt aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740
aaaaaaaaaa aaaaaaaaaa aaaaaaattt t 1771

```

<210> 50

<211> 397

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (201)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (207)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (352)

<223> n equals a,t,g, or c

<400> 50

```

gggtcgaccc acgcgtccgc tcgctccggg atcgcccgcg ctagagacgc atagcgtct 60
aatcgctcgc acgcaccggc cctcgctcgc tcgcccgtcc gtgcccgcgc cgccagccc 120
accgccaccc tttgcagcca tgtccaccag gtcygtgtcc tcgtcytcct accgcagatg 180
ttcgcgggc ccggcaccgg naggcgnccg agtccacgc gcataacgtg accagtccac 240
ccgcacctac agcctgggca gcgcctgcgc ccagcacca gccgcagcct ctamamctcg 300
tccccggcg gcgcgtatgt tcacggctcc ttccggggtg cgcctgcgga anatgttgcc 360
ccggcggtgc gcttgctggc aggattccgt ggaattt 397

```

<210> 51  
<211> 1635  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1422)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1617)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1620)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1629)  
<223> n equals a,t,g, or c

<400> 51  
gccacgcgt cgcgccacgc gtccgcccac gcgtccgcct ctccagccct tctcctgtgt 60  
gcctgcctcc tgccgcccgc accatgacca cctccatccg ccagttcacc tcctccagct 120  
ccatcaaggc ctcctccggc ctggggggcg gctcgcccg caccctcctgc cggctgtctg 180  
gcggcctggg tgccggctcc tgccagctgg gatctgctgg cggcctgggc agcaccctcg 240  
ggggtagcag ctactccagc tgctacagct ttggctctgg tgggtggctat ggcagcagct 300  
ttgggggtgt tgatgggctg ctggctggag gtgagaaggc caccatgcag aacctcaatg 360  
accgcctggc ctcctacctg gacaaggctg gtgccctgga ggaggccaac actgagctgg 420  
aggtgaagat ccgtgactgg taccagaggc agggcccggg gcccggccgt gactacagcc 480  
agtactacag gacaattgag gagctgcaga acaagatcct cacagccacc gtggacaatg 540  
ccaacatcct gctacagatt gacaatgccc gtctggctgc tgatgacttc cgcaccaagt 600  
ttgagacaga gcaggccctg cgcctgagtg tggaggccga catcaatggc ctgcgcaggg 660  
tgctggatga gctgaccctg gccagagccg acctggagat gcagattgag aacctcaagg 720  
aggagctggc ctacctgaag aagaaccacg aggaggagat gaacgccctg cgaggccagg 780  
tgggtggtga gatcaatgtg gagatggacg ctgcccagg cgtggacctg agccgcattc 840  
tcaacgagat gcgtgaccag tatgagaaga tggcagagaa gaaccgcaag gatgccgagg 900  
attggttctt cagcaagaca gaggaactga accgcgaggt ggccaccaac agtgagctgg 960  
tgcagagtgg caagagtgag atctcggagc tccggcgac catgcaggcc ttggagatag 1020  
agctgcagtc ccagctcagc atgaaagcat ccctggaggg caacctggcg gagacagaga 1080  
accgctactg cgtgcagctg tcccagatcc aggggctgat tggcagcgtg gaggagcagc 1140  
tggcccagct tcgctgcgag atggagcagc agaaccagga atacaaaatc ctgctggatg 1200  
tgaagacgcg gctggagcag gagattgcc aataccgccc cctgctggag ggagaggatg 1260  
cccacctgac tcagtacaag aaagaaccgg tgaccaccgg tcagggtgcgt accattgtgg 1320  
aagaggtcca gcatggcaag gtcattctct cccgcgagca ggtccaccag accaccgct 1380  
gaggactcag ctaccccgcc cggccaccca ggaggcaggg angcagccgc cccatctgcc 1440  
ccacagtctc cggcctctcc agcctcagcc ccctgcttca gtcccttccc catgcttctc 1500

```
tgcctgatga caataaagct tgttgactca gctaaaaaaa aaaaaaaaaa aaaaaaaaaa 1560
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaanttn 1620
gggggggggnc ccccc                                     1635
```

<210> 52

<211> 1780

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1780)

<223> n equals a,t,g, or c

<400> 52

```
ccgccgccgc cgccgccgcc ggagctctgt agtatggcat cgaggagaat ggagaccaa 60
cctgtgataa cctgtctcaa aacctcctc atcatctact ccttcgtctt ctggatcact 120
ggggtgatcc tgcctggctgt tggagtctgg ggcaaaactta ctctgggcac ctatatctcc 180
cttattgccg agaactccac aaatgtcccc tatgtgctca tcggaactgg caccactatt 240
gttgctcttg gcctgttttg atgctttgct acatgtcgtg gtagcccatg gatgctgaaa 300
ctgtatgcca tgtttctgtc cctgggtgtc ctggctgagc tcgtagctgg catttcaggg 360
tttgtgtttc gtcattgagat caaggacacc ttcctgagga cttacacgga cgctatgcag 420
acttacaatg gcaatgatga gaggagccgg gcagtggacc atgtgcagcg casctgagct 480
gctgtggtgt gcagaactac accaactgga gcaccagccc ctacttcctg gagcatggca 540
tccccccag ctgctgcatg aacgaaactg attgtaatcc ccaggatcta cacaatctga 600
ctgtggccgc caccaaagtt aaccagaagg gttgttatga tctggtaact agtttcatgg 660
agactaacat gggaatcatc gctggagtgg cgtttggaat cgcattctcc cagttaattg 720
gcatgctgct ggccgtgctg ctgtcccggg tcatcacggc caatcagtat gagatggtgt 780
aaggagaagt ctttcaagaa tgacggaata agagacctgt tttaaaaagg aactgcagca 840
atctttgaaa gacttccaaa gaatgttaga gcacagtaca taatacactt gccctgctcc 900
ctctmccctt taccacaaa cgtgcaactg acactcccac ccagtctctg ctccaccttt 960
cagcccacgt cacgtgtagt gtccattttg tgaagccctg ttgtgccaca gagtgtagcc 1020
aggccccctt gcagctagtc ctagtgaacc tcaccccag gccctgcatg ggcmrgcccc 1080
tccatctgta cttggtccaa ctgcaactca tcatcgggtg ctgggttatca caccatcgct 1140
ggcccccttg ggccctgcat gtagtgtggg aggctcctgt tagctcctca ctgtggtaaa 1200
tgccacacac ctttaagtag ataagcagac gatagttatc tgttcttttg acttaatctc 1260
at ttgggttg attttccctc tactaaggct ttcctacctt cttcaggctg cctaagacat 1320
gtaacgaaac acttcaataa ttgtccatga ggagaaaaaa agcatgtgtc atgcatgaag 1380
gaaactgaac ttgaggtggc ctccctgctt gttacatacc tgggtatgtg taggcagttt 1440
agtgcattct tgccctctcag ttgaaacctg tataaccctg ttacaaaagc gtgttggtgc 1500
ttcttgatga ggccatgata ttttggtttt ccccaattaa ttgctattgt gttattttac 1560
tacttctctc tgtatttttt cttgcattga cattatagac attgaggacc tcatccaaac 1620
aatttaaaaa tgagtgtgaa gggggaacaa gtcaaaatat ttttaaaaga tcttcaaaaa 1680
taatgcctct gtctagcatg ccaacaagaa tgcattgata ttgtgaacat ttgtgatata 1740
tgtattaata aatagagcaa ttacaagcaa aaaaaaatgn                                     1780
```

<210> 53

<211> 490

<212> DNA

<213> Homo sapiens

<400> 53  
aattcggcag agaattttca tgagtcgcct tcaaaactct cgtgtagggt tgacaatgtg 60  
gggggggtgg ggatccagct tattctttta ttttcaagtc cattcttggg gctggtggg 120  
aggcaggaga ataccctcc ctaagccctt agtgtgtgcc gagcttgctt tgtgatgtg 180  
gcaggggagg ggagacctgg gtggtgactg agttcccttt atcaaaccct tcaatgggca 240  
caaaattgag tgcttgattt taggttttat tttttatga atgtccaaat ctgtgtttcc 300  
ccctgccctc ccagactgtg tggccagtgt aaagtgtctg gtttgtgttc atctctccct 360  
catttctgga gcagggcctg agaccctgcc acatctccta tgctctgcat ccacgcctct 420  
tttgacatt aaaggttgat tgatgcaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480  
aaaaaaaaa 490

<210> 54  
<211> 1944  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (466)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (634)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1308)  
<223> n equals a,t,g, or c

<400> 54  
acggtacgga attcccgggt cgacccacgc gtccgacccc ggacccggag tcgcgagag 60  
ctgggcagtg ttggccgctg gcggagcgtt ggggcagcat gaagtgcctg gtcacgggcg 120  
gcaacgtgaa ggtgctcggc aaggccgtcc actccctgtc ccgcacggg gacgagctct 180  
acctggaacc cttggaggac gggctctccc tccggacggt gaactcctcc cgctctgcct 240  
atgcctgctt tctctttgcc ccgctcttct tccagcaata ccaggcagcc acccctggtc 300  
aggacctgct gcgctgtaag atcctgatga agtctttcct gtctgtcttc cgctcactgg 360  
cgatgctgga gaagacggtg gaaaaatgct gcatctccct gaatggccgg arcagccgcc 420  
tggtggtcca gctgcattgc aagttcgggg tgcggaagat camaanctgt ccttcmagga 480  
ctgtgagtcc ctgcaggccg tcttcgaccc agcctcgtgc cccacatgc tccgcgcccc 540  
agcacgggtt ctgggggarg ctgttctgcc cttctctcct gcaactggctg aagtgcgct 600  
gggcattggc cgtggcgag gktcatcctg gcantaccac gaggaggagg cagacagcac 660  
tgccaaagcc atggtgactg agatgtgcct tggagaggag gattccagc agctgcaggc 720  
ccaggaaagg gtggccatca cttctgcct caaggaattc cgggggctcc tgagctttgc 780  
agagtcagca aactgaatc ttagcattca ttttgatgct ccaggcagge ccgccatctt 840  
caccatcaag gactctttgc tggacggcca ctttgtcttg gccacactct cagacaccga 900  
ctgcgactcc caggacctgg gctccccaga gcgtcaccag ccagtgcctc agctccaggc 960  
tcacagcaca cccccccgg acgactttgc caatgacgac attgactctt acatgatcgc 1020  
catggaacc actataggca atgagggtc gcgggtgctg ccctccattt ccctttcacc 1080  
tggccccag ccccccaaga gccccggtcc ccactccgag gaggaagatg aggetgagcc 1140

```

cagtacagtg cctgggactc cccaccccaa gaagttccgc tcaactgttct tcggtccat 1200
cctggcccct gtacgctccc cccagggccc cagcctgtgc tggcggaaga cagtgaggg 1260
gaaggctgaa ccaagaacct gaagcctgta cccagaggcc ttggactnag acgaagcccc 1320
agccagtggc agaactgggt ctctcagccc tggggatcag aaaggtgggc ttgctggagc 1380
tgagctgttt cactgcctct cgcaggcccc agctggctgt cactgtaaag ctgtcccaca 1440
gcggtcgggc ctgggccgtt atctccccac aamccccarc caatcaggac tttccagact 1500
tggccctgaa ctactgacgt tcctacctct tatttctcat tgagcctcag gctatactcc 1560
agctggccaa ggctggaac ctgtctccct caggctcacc ttcctaagga aaatgtcata 1620
gtaggtgctg ctggcccctg gtgatccagc ttctctgcca atcatgacct gtctcttct 1680
gaagtcctgg gcatgcatct gggacccccg tggagctgac aagttttcct tgctttcctg 1740
atactctttg gcgtgactt ggaattctaa gagccttga cccgagtgtg tggctaggg 1800
tgccctggct ggggcccggg gccgagactc ccaagcggst ctgtgcagaa gagctgccag 1860
gcagtgtctt agatgtraga cggaggccat ggcgagaatc cagctttgac ctttattcaa 1920
gagaccagat gggtttgccc cagg                                     1944

```

<210> 55

<211> 994

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (896)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (971)

<223> n equals a,t,g, or c

<400> 55

```

ccccgtgcg cagtaccggg tccgcgcctg tccccgaaac ttgcacccc gtcgaactct 60
cgcgagagcg ktatctgctg gtccggacgt gcggaggctc tcactttccg tcatggcgct 120
gaaggtagcg accgtcgccg gcagcgccgc gaaggcgtgc tcgggccagc ccttctctgc 180
cgtccctggg aggttctagg cgcacacgag gtcccctcga ggaacatctt ttcagaacaa 240
acaattcttc cgtccgctaa gtatggcggg cggcacacgg tgaccatgat cccaggggat 300
ggcatcgggc cagagctcat gctgcatgtc aagtcctgtc tcaggcacgc atgtgtacca 360
gtggactttg aagaggtgca cgtgagttcc aatgctgatg aagaggacat tcgcaatgcc 420
atcatggcca tccgccggaa ccgcgtggcc ctgaagggca acatcgaaac caaccataac 480
ctgccaccgt cgcacaaatc tcgaaacaac atccttcgca ccagcctgga cctctatgcc 540
aacgtcatcc actgtaagag ccttccaggc gtggtgaccc ggcacaagga catagacatc 600
ctcattgtcc gggagaacac agaggcgag tacagcagcc tggagcatga gagtgtggcg 660
ggagtgggtg agagcctgaa gatcatcacc aaggccaagt ccctgcgcgt tgccgagtat 720
gccttcaagc tggcgagga gagcgggcgc aagaaagtga cggccgtgca caaggccaac 780
atcatgaaac tgggcgatgg gcttttcctc cagtgtgca gggagggtgc agccggttac 840
cctcagwtca ccttcgagaa catgattgtg gataacacca ccatgcagct ggtgtncgg 900
ccccagcagt ttgatgtcat ggtgatgcc aatctctatg gcaacatcgt caaacaatgt 960
ctgcgcggga ntggtcgggg gcccaagctt gttg                                     994

```

<210> 56

<211> 328

<212> DNA  
<213> Homo sapiens  
  
<220>  
<221> misc feature  
<222> (123)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (156)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (170)  
<223> n equals a,t,g, or c

<400> 56  
gggtcgaccc acgcgtccgc ccacgcgtcc ggatgacttc attgccaaag ttgttcaaag 60  
gtagccttgg ccctttttca tctgagtcgc atttagagat gtataaagaa tgttgttgag 120  
tanggcgcgg tggtcacgc ctgtaatccc cacacnttgg gaaggccgan gcaggcggat 180  
cacgaggtca gaagattgag accattctgg ctaacatggt gaacccccat ctctactaaa 240  
aatacaaaaa ttagtcaggc gcgatggcgg gcacatgtag taccagctac tcgggagggt 300  
gatgcagaag aataacttgg aacctggg 328

<210> 57  
<211> 1489  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (710)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1109)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1117)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1206)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1211)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1218)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1264)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1311)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1446)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1467)  
<223> n equals a,t,g, or c

<400> 57  
cggcacgagg ggtggtgtgg gtgtgttttag aaaaaagatg cattcctgaa gatctctggt 60  
gctgaagggc ctcgagttcc ttccagagac tgtatttgac acacttttagg tacacacaaa 120  
cgaatggtat cacatgcaat attttaatgg agcaatggga gaggctcttt gaaatgggg 180  
ttgcatcttt ttgtaacatt ttgatttctc tgggtgcctta ttctacttg atgctggcac 240  
tcacataccc acaagaagct gacacagaag tcagccttag gcgtggggac atatgggtga 300  
tgtttgagca tgcagggggc atggggagtt tgggtgtcagt tgggtggagaa gggactagat 360  
ggcatctctt agccgaggcc aacaggaact gcacaagtcc attatagtca aagttagcaa 420  
ttttgatacg taaacacaat acttcattct tcctcatctg agctttcctt ccttcttcct 480  
tttctatctc taccttctca taaagggtgct gctgctgctg ctaagggtgcc cggagtccag 540  
aatgtccatt aatcactcag gcacgagcct ggcaactgcc cgtcagcccc cagcatgacc 600  
aaacccaggt ttctcttgct tggggctgag aactgtcaga tttttctcat caaaaatggt 660  
ttccaaggaa tcagtggatt acagtttttc tgcattgaaa atgcactttn aaaaaataaa 720  
ttaaagctcc agactgttta aaatatacag agggagcagg ggaaagttaa gcatgtgcta 780  
gtgtctgaac ccagttcagt ttatctccag ttgaaacgat atacactata ttatgtataa 840  
atgtatacac acttcctata tgtatccaca tatatatagt gtatatatta tacatgtata 900  
ggtgtgtata tgtgcatata tacacacatg cacataacaa aatcagatgc tcattacaaa 960  
tccagatgct cattacaaaa ccagatgcta cacaacagc agcagaggaa acaagggttg 1020  
actcttgcaa cagatcacia aaaataaaaa cagctacttg cagtgaacttt ggtcatttct 1080  
gtatgttcat aaagaatgga tttgtaacna ggaaaaanaag gaccagtgtt agtgaaaagg 1140  
gaagatgggg cgaaccatct tgatccgatg cgaatccgta atgggtctata tacatttcat 1200



cagtantcat ntagtcangt gattgattca gttctgctat gaaacattgt aacacgtacc 1260  
cacnactgac aactactcgt gagcggtcat taggagtgac ctaactttgc ntgcctgctc 1320  
atgggacgag ctcccttaggt ggagataccg gggaaatagag aaagatgcac gtctctgcgt 1380  
tgctcgctgc tttgaggggc ggtctttacc ttccgtgttg gagtcctccc tgagtcgggc 1440  
gctggntgcg ggacacggcc cttctcngtg tcccagggcg tgcctcatt 1489

<210> 58

<211> 1283

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (38)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (550)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1242)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1250)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1260)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1263)

<223> n equals a,t,g, or c

<400> 58

aggtaatttg aattgagaga gagtaagtga cttgctgnaa aaaggggttaa tcaacagcag 60  
agctgggatt tgaaccata actctgtcaa agcctccact cctaactcct gttcatgctc 120  
ctgtggagaa aatgcttgta gtaacatatt ttaaattgtac taacaagacc agtcatgggm 180  
aaatgtttct gagacaaatc tctagtttat gatttaaaac agtacgtttt cttacgtgac 240  
gaaaacaaaa agtgtgttaa tttgttccca gtggttgaag ttatttgcca acaattttac 300  
tgtttctctt catctgttta taggatttct ctgcctcttc caaacttttc ctccctgaac 360  
ctgaggggta agcattttat ttcccttttag gaaaaacgtc agctgcttgt aaccactgtg 420  
tttatgtcaa agcattcatt ttttttagga tatctgaaaa aatgccatat aagaraaaam 480  
tctataaaac atctatwatt ttcgaacca agtacactct tgcattctaw gctttaagtt 540

```

aaatgcaaan tcctttttcc ttcttcctgc tgcaagtact atctcatcct gatgctcaag 600
agtgtcaggg cctgggtttc caaacagaga ctaccctaaa attatttggc gagtagtact 660
ttacacaatt gcctctcccc cacaaatcat aattgtttca gtaaaatggg tacttggttt 720
ttccaagaaa aaactcgttt ttactcattt ttggcctggt tgtttattta gaaactaatc 780
tggtattcact ccctctggtt gataccctact caaaaaggac acttctgatt aagacgggtg 840
aaactagaga tggacaggtt atcaacgaaa cttctcagca tcacgatgac cttgaataaa 900
aattgcacac actcagtgcg gcaatatatt accagcaaga ataaaaaaga aatccatata 960
ttaagaaac agctttcaag tgcttttctg cagtttttca ggagcgcaag atagatttgg 1020
aataggaata agctctagtt cttaacaacc gacactccta caagatttag aaaaaagttt 1080
acaacataat ctagtttaca gaaaaatctt gtgctagaat acttttttaa aggtattttg 1140
aataccatta aaactgcttt tttttttcca gcaagtatcc aaccaacttg gttctgcttc 1200
aataaatctt tggaaaaact maaaaaaam mngggggggn gcccggggtn 1260
ccnccggggg gcccaagttt tac 1283

```

<210> 59

<211> 740

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (696)

<223> n equals a,t,g, or c

<400> 59

```

agaaggagcg cggggaggac gtaccttgtg agatgcgagc cggccaacag cttgcaagca 60
tgctccgctg gacccgagcc tggaggctcc cgcgtgaggg actcggcccc cacggcccta 120
gcttcgcgag ggtgcctgtc gcaccagca gcagcagcg cggccgaggg ggcgccgagc 180
cgaggccgct tccgctttcc tacaggcttc tggacgggga ggcagccctc ccggccgctc 240
cttttttgca cgggctcttc ggcagcaaaa ctaacttcaa ctccatcgcc aagatcttgg 300
cccagcagac aggccgtagg tgctgacggt ggatgctcgt aaccacggtg acagccccc 360
cagcccagac atgagctacg agatcatgag ccaggacctg caggaccttc tgccccagct 420
gggcctggtg ccctgcgctg tcgttgcca cagcatggga ggaaagacag ccatgctgct 480
ggcactacag aggccagagc tgggtggaac tctcattgct gtagatatca gccagtgga 540
aagcacaggt gtctcccact ttgcaacctt tgtggcagcc atgagggcca tcaacatcgc 600
agataggctt gccccgctcc cgtgcccga aactggcgga tgaacagctc agttctgtca 660
tccaggacat ggccgtgcgg cacacttgct tcaatnaacc tggtagaggt agacgggcgt 720
tttcgtgttg gaggtgga 740

```

<210> 60

<211> 1291

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (7)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (147)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1211)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1283)

<223> n equals a,t,g, or c

<400> 60

```
acttttnccc ctcccccttt cctttcccggt ctcacgcgcc aggccgcttg cacatgcgca 60
ttaggtacaa agcctcgctc tttgtcccca tctgtcgttc acacgaactc aagcctttgg 120
cattcggcag ccaatagaat ctaaganatg gcggaaaaat gattccgcct cgggagctaa 180
acttgattgg cagtttagct aaccaatcga gaacgccatt tgtamccctt ggcaggcamc 240
gagctccgtc gtctcgtttc cggcggtcgc gcgctctttt ctggggacgg gagaggccgt 300
gtagcgtcgc cgttactccg aggagatacc agtcggtaga ggagaagtcg aggttagagg 360
gaactgggag gcactttgct gtctgcaatc gaagttgagg gtgcaaaaat gcagagtaat 420
aaaactttta acttgagaa gcaaaaccat actccaagaa agcatcatca acatcaccac 480
cagcagcagc accaccagca gcaacagcag cagccgccac caccgccaat acctgcaaat 540
gggcaacagg ccagcagcca aaatgaaggc ttgactattg acctgaagaa ttttagaaaa 600
ccaggagaga agaccttcac ccaacgaagc cgtctttttg tgggaaatct tcctcccgac 660
atcactgagg aagaaatgag gaaactatct gagaaatatg gaaaggcagg cgaagtcttc 720
attcataagg ataaaggatt tggctttatc cgcttggaac cccgaaccct agcggagatt 780
gccaaagtgg agctggacaa tatgccactc cgtggaaagc agctgcgtgt gcgctttgcc 840
tgccatagtg catcccttac agttcgaaac ctctctcagt atgtgtccaa cgaactgctg 900
gaagaagcct tttctgtgtt tggccaggta gagagggtg tagtcattgt ggatgatcga 960
ggaaaggcct caggaaaagg cattgttgag ttctcaggga agccagctgc tcggaaagct 1020
ctggacagat gcagtgaagg ctcccttcctg ctaaccacat ttctcgtcc tgtgactgtg 1080
gagcccatgg accagttaga tgatgaagag ggacttccag agaagctggg tataaaaaac 1140
cagcaatttc acaaggaacg agagcagcca cccagatttg cacagcctgg ctcccttkga 1200
gtatgaatat ngccatgcgc tgggaaggca ctcattgaga tggagaaagc agcctggggg 1260
gacaagaagt gaagactcct gnttccaaaa a 1291
```

<210> 61

<211> 971

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (856)

<223> n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (886)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 61

```

ctgcagtacc ggtccggaat tcccgggtcg acccacgcgt ccgggtctgt ggtcctctct 60
cggctcctcg cggctcgcgg cgcccgacgg ttccctgggac acctgcttgc ttggcccgtc 120
cggcggtcga gggcttctct gctgcgctcc cggttcgctg gacgggaaga agggctgggc 180
cgtcccgtcc cgtcccctc ggaaccccaa gtgcgcgcgc tgacctgctg cagggcgaga 240
tgagcgcgga cgcagcgggc ggggcgcccc tgccccggct ctgctgcctg gagaagggtc 300
cgaacggcta cggcttcac ctgcacgggg agaagggcaa gttgggccag tacatccggc 360
tggtggagcc cggctcgccg gccgagaagg cggggctgct ggcgggggac cggctggtgg 420
aggtgaacgg cgaaaacgtg gagaaggaga cccaccagca ggtggtgagc cgcattccgcg 480
ccgcactcaa cgccgtgcgc ctgctggtgg tcgaccccg gacggacgag cagctgcaga 540
agctcggcgt ccaggctcga gaggagctgc tgcgcgccca ggaagcgccg gggcaggccg 600
agccgcccgc cgccgccrag gtgcaggggg ctggcaacga aaatrarcct cgcraggccg 660
acaagagcca cccggagcag cgcgagcttc ggcctcggct ctgtaccatg aagaagggcc 720
ccagtggcta tggcttcaac ctgcacagcg acaagtccaa gccaggccag ttcattccgt 780
cagtggacct agactccccg gctgaggctt cagggtccg ggcccaggat cgcattgtgg 840
aggtgatgct tctcgnctt ctctctatct gaactgcccc caaccnctgc agattagcag 900
caccttgggg cagccatcat accatcatgg ggtttgatta gcccacgggc attagccaac 960
ctgggaggtt g                                     971

```

&lt;210&gt; 62

&lt;211&gt; 618

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (563)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (598)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 62

```

gggtcgaccc acgcgtccgg cagaaatgaa ggaccacctg ccaagacgaa gagctgggtg 60
ggacccacgc tgcattttca tcgaaagagt gaacatctag tgggactgaa agttctttgt 120
tgtttcagat tgtagagtgt gattgatgga attggtctgt ggaattgca ttgtttttat 180
ttctttatgt aatcagttta agtaataggg ggtatatata atcgtaagta ttttaggggtg 240
ggaggggcta ttaagtaatt aagtgggtgg ggttagttta aaagttagca tgatatgtat 300
tagataactc tataagtga catgtgtact tacttgtgat cctttaccct atgattgcta 360
cccttaacga ttcaaataa actcagaggg aactgcaggg agatcaaacc atttagggca 420
aattggacat gaataaaact ctagtgggaa aaagttcaaa ggtgattgaa taaataattt 480
aactttgccc tgggtattaa gtccagggct cccagattgt ggagcagagc cttggagagt 540
acaggatgaa ggagatagat gcncctttga cttgccggga atgaaattgg attaatgnaa 600

```

ggatggtaaa taattcca

618

&lt;210&gt; 63

&lt;211&gt; 1138

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (7)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (15)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (22)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (27)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (29)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1123)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 63

tctatanatc atganaggaa anggtancng acagtacggt cggattcccg ggtcgaccca 60  
cgctccgatg acttcacccc tctggagatc ctctggacct tctccatcta cctggagtca 120  
gtggccatct tgccgcagct gttcatggtg agcaagaccg gcgaggcggg gaccatcacc 180  
agccactact tgtttgcgct aggcgtttac cgcacgctct atctcttcaa ctggatctgg 240  
cgctaccatt tcgagggctt cttcgacctc atcgccattg tggcaggcct ggtccagaca 300  
gtcctctact gcgatttctt ctacctctat atcaccaaag tcctaaaggg gaagaagttg 360  
agtttgccgg catagccccg gtcctctcca tctctctcct cggcagcagc gggaggcaga 420  
ggaaggcggc agaagatgaa gagctttccc atccaggggt gactttttta agaaccacc 480  
tcttgtgctc cccatcccgc ctctgcggtg gtttcagggtg gacagtggag gatccaggtc 540  
ttggggagct caggacttgg gctgtttgta gttttttgcc ttttagacaa gaaaaaaaaa 600  
tctttccact ctttagtttt tgattctgat gactcgtttt tcttctactc tgtggcccca 660  
atttttataa agtggttttg agtgcctat gggcgggggc agggccaag atcttttccc 720  
ttcccaggc ccctcggtc cctcccagat cccaccccca gcccactgg ttgccaaca 780

ctaaatctgc cgacacccat ctgccccacc tcctgccatg gccatgaacc gcgaccccca 840  
ctaaatttct agattgggga tagggagaaa gggaggccca ggaaggtctc ccctgatttt 900  
tttcatagtg aatttttttc ccagagttt gaattttttg gtcttctcct ggttttttgg 960  
caaattaggg gggcccgagg ctcaagtgcg ggaagggggc tggcccgagg atcccatggc 1020  
tctcacacca tgtttttgta cagaactgat ggttgaatct ttgttctctt gaaataaaca 1080  
gaagaaaatg aaaccttaaa aaaaaaaaaa aaaaaaaaaa acncgggggg gggcccg 1138

<210> 64

<211> 418

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (365)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (371)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (380)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (391)

<223> n equals a,t,g, or c

<400> 64

tgctcatcca gaggagctca ccacagtcac tgcgacagac tgccacactc accctggcct 60  
ggcctcagag aagttgagct actggcctca gtacacacag agcagatgga ggaagagctg 120  
gcactaggac ccagggggca ggggggagcc tccctggctg gaagggatgg caggagcgct 180  
ggtgcaggta gctatggagc tctggccaac tctgcctggg gaggtcccag gaaggtggcg 240  
tcagcatctg cagccgcgtc gacgttgctg gagcctccgc ggaggacca ggagagccgg 300  
actaggacca gggccctggg cctccccaca ctcccatgg agaagctggc ggcctctaac 360  
agagncccaa ngggcttggg cggtcctggg ncgtgaaaat gttcaagtgc ccgattga 418

<210> 65

<211> 2836

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2834)

<223> n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (2836)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 65

```
aagaaaccgc ccattacaca cccaggtaca ccagcagagg aaacttataa cctcgggagg 60
caggtccttc ccctcagtgc ggtcacatac ttccagaaga gcggaccagg gctgctgcc 120
gcacctgcca ctgagagcgc ctctgtcgct gggacccttc agaactctct ttgctcaca 180
gttaccaaaa aaaaaagagc caacatgttg gtattgctgg ctggtatctt tgtggtccac 240
atcgctactg ttattatgct atttgttagc accattgcc  atgtctggtt ggtttccaat 300
acggtagatg catcagtagg tctttggaaa aactgtacca acattagctg cagtgcacgc 360
ctgtcatatg ccagtgaaga tgccctcaag acagtgcagg ccttcattgat tctctctatc 420
atcttctgtg tcattgccct cctggctctc gtgttccagc tcttcaccat ggagaaggga 480
aaccggttct tcctctcagg ggscaccaca ctggtgtgct gsctgtgcat tcttgtgggg 540
tgtccatcta cactagtcat tatgcgaatc gtgatggaac gcatatgcac cacggctatt 600
cctacatcct gggtcggatc tgcttctgct tcagcttcat catcggcgtt ctctatctgg 660
tcctgagaaa gaaataaggc cggacgagtt catggggatc tgggggggtg ggaggaggaa 720
gccgttgaat ctgggaggga agtggaggtt gctgtacagg aaaaaccgag ataggggagg 780
ggggaggggg aagcaaggga gggaggtcaa atcccaaacc attactgagg ggattctcta 840
ctgccaagcc cctgccctgg ggagaaaagta gttgctagt actttgatgc tcccttgatg 900
gggtccagag agcctccctg cagccaccag acttggcctc cagctgttct tagtgacaca 960
cactgtctgg ggccccatca gctgccacaa caccagcccc acttctgggt catgcactga 1020
gggtccacaga cctactgcac tgagttaaaa tagcgggtaca agttctggca agagcagata 1080
ctgtctttgt gctgaatacg ctaagcctgg aagccatcct gcccttctga cccaaagcaa 1140
aacatcacat tccagtctga agtgccctact ggggggcttt ggctgtgag ccattgtccc 1200
tctttggaac agatatttag ctctgtggaa ttcagtgcac aaatgggagg aggaaagaga 1260
gtttgtaagg tcatgctggt ggggttagcta aaccaagaag gagaccttt cacaatggaa 1320
aacctggggg atggtcagag cccagtcgag acctcacaca cggctgtccc tcatggagac 1380
ctcatgccat ggtctttgct aggcctcttg ctgaaagcca aggcagctct tctggagttt 1440
ctctaaagtc actagtgaac aattcggtag taaaagtacc acacaaacta tgggatccaa 1500
ggggcagctc tgcaacagtg ccattgttagg gttatgtttt taggattccc ctcaatgcag 1560
tcagtgtttc ttttaagtat acaacaggag agagatggac atggctcatt gtagcacaat 1620
cctattactc ttctctaac atttttgagg aagttttgtc taattatcaa tattgaggat 1680
cagggctcct aggtcagtg gtagctctgg cttagacacc acctggagtg atcacctctt 1740
ggggaccctg ctatccca ttcacagggt aggcattggca attctggaag ctgattaaaa 1800
cacacataaa ccaaaaccaa acaacaggcc cttgggtgaa aggtgctata taattgtgaa 1860
gtattaagcc taccgtatct cagccatgat aagaacagag tgcctgcatt cccaggaaaa 1920
tacgaaaatc ccattgagata aataaaaaata taggtgatgg gcagatcttt tctttaaata 1980
aaaaaagcaa aaactctgt ggtacctagt cagatggtag acgagctgtc tgcctgcgca 2040
ggagcacctc tatacaggac ttagaagtag tatgttattc ctggttaagc aggcattgct 2100
ttgccctgga gcagctatct taagccatct cagattctgt ctaaaggggt tttttgggaa 2160
gacgttttct ttatcgccct gagaagatct accccaggga gaatctgaga catcttgctt 2220
acttttcttt attagctttc tcctcatcca tttcttttat accttctctt tttggggagt 2280
tgttatgcca tgatttttgg tatttatgta aaaggattat tactaattct atttctctat 2340
gtttattcta gttaaggaaa tgttgagggc aagccaccaa attacctagg ctgagggttag 2400
agagattggc cagcaaaaac tgtgggaaga tgaactttgt cattatgatt tcattatcac 2460
atgattatag aaggctgtct tagtgcaaaa aacatactta catttcagac atatccaaag 2520
ggaatactca cattttgtta agaagttgaa ctatgactgg agtaaacctt gtattccctt 2580
atcttttact tttttctgt gacatttatg tctcatgtaa tttgcattac tctgggtgat 2640
tgttctagta ctgtattggg cttcttcgtt aatagattat ttcatactat ataattgtaa 2700
```

```

atattttgat acaaattgtt ataactctag ggatataaaa acagattctg attcccttca 2760
tttgttgaat gtttttttct aaaaaaaatg tggagaaata tggataatta tgacatttat 2820
ccctcattaa agcngn                                     2836

```

<210> 66

<211> 2305

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1973)

<223> n equals a,t,g, or c

<400> 66

```

aaacgttccc ggtccttcct gaaccaagct gtggaccctc gtaagcaacc cggacaccga 60
cgcgctcatc tgctggagcc cgagcgsгаа cagcttccac gtgttcgacc agggccagtt 120
tgccaaggag gtgctgcca agtacttcaa gcacaacaac atggccagct tcgtgcggca 180
gytcaacatg tatggcttcc ggaaagtggg ccacatcgag cagggcgkcc tgggtcaagcc 240
agagagagac gacacggagt tccagcacc atgcttcctg cgtggccagg agcagctcct 300
tgagaacatc aagaggaaag tgaccagtgt gtccaccctg aagagtgaag acataaagat 360
ccgccaggac agcgtcacca agctgctgac ggacgtgcag ctgatgaagg ggaagcagga 420
gtgcatggac tccaagctcc tggccatgaa gcatgagaat gaggctctgt ggcgggaggt 480
ggccagcctt cggcagaagc atgccagca acagaaagtc gtcaacaagc tcattcagtt 540
cctgatctca ctggtgcagt caaaccgat cctgggggtg aagagaaaга tccccctgat 600
gtgaacgac agtggtcag cacattccat gcccaagtat agccggcagt tctccctgga 660
gcacgtccac ggctcgggccc cctactcggc cccctcccca gcctacagca gctccagcct 720
ctacgcccct gatgctgtgg ccagctctgg acccatcatc tccgacatca ccgagctggc 780
tcctgccagc cccatggcct ccccgccgg gagcatagac gagaggcccc tatccagcag 840
ccccctggtg cgtgtcaagg aggagcccc cagcccgcc yagagcccc gggtagagga 900
ggcaggtccc gggsgcccat ctcccggtga caccctcttg tccccgaccg ccctcattga 960
ctccatctcg cgggagagtг aacctgcccc cgsctccgtc acagccctca cggacgccag 1020
gggccacacg gacaccgagg gccggcctcc ctccccccg cccacctcca cccctgaaaa 1080
gtgcctcagc gtasctgcct ggacaagaat gagctcagtg accacttgga tgctatggac 1140
tccaacctgg ataacctgca gacctgctg agcagccacg gcttcagcgt ggacaccagt 1200
gccctgctgg acctgttcag cccctcggtg accgtgcccг acatgagcct gcctgacctt 1260
gacagcagcc tggccagtat ccaagagctc ctgtctcccc aggagcccc caggcctccc 1320
gaggcagaga acagcagccc ggattcaggg aagcagctgg tgcactacac agcgcagcgc 1380
tgttcctgct ggaccccggc tccgtggaca ccgggagcaa cgacctgccg gtgctgtttg 1440
agctgggaga gggctcctac ttctccgaag ggacggcttc gcaaggгacc ccaccatctc 1500
cctgctgaca ggctcggagc ctcccaaagc caaggacccc actgtctcct agaggccccг 1560
gaggagctgg gccagccgcc cacccccacc cccagtgcag ggctggtctt ggggaggcag 1620
ggcagcctcg cggctctggg cactggtggg tcggccgcca tagccccagt aggacaaacг 1680
ggctcgggtc tgggcagcac ctctggtcag gagggtcacc ctggcctgcc agtctgcctt 1740
cccccaaccc cgtgtcctgt ggtttggttg ggcttcacag ccacacctgg actgacctg 1800
caggttgttc atagtcaгаа ttgtattttg gatttttaca caactgtccc gttccccгct 1860
ccacagagat acacagatat atacacacag tggatggacг gacaagacag gcagagatct 1920
ataaacagac aggtctctat ctatggcctc catgtgtttc ctctgtccca ggntggtgct 1980
gtggttggtg ctgcaatgag gaggggcccc gggcacagaa gggccgggct gcagtggcct 2040
cctgggggaa gacggatggt gcagctagct ccgtgcctgc ccgactcccc aggaccagca 2100
tgtgcttgca gttctttatt gagggaccag gggtgggcgc ctcacctgg ccctgggggt 2160

```



```

ctctggttgt cacaggacca ccaggaaccc ccttcccaag gtgttcgcac tcggacaggt 2220
gatgcggggc gggcacactg tctttctgcc agagccagca ccctgtgtag gcacggggaa 2280
cgggagcctg tcccgtagct ttagg                                     2305

```

```

<210> 67
<211> 1907
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (1221)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (1655)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (1896)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (1904)
<223> n equals a,t,g, or c

```

```

<400> 67
gacgcccgcc gcctcactgt ttctagcctt cagtggccaa cgttggtagt cattgtgacc 60
tcagcctgaa aatccctgaa attagcatcc aggatatgac agcccagggtg accagcccat 120
cgggcaagac ccattgaggcc gagatcgtgg aaggggagaa ccacacctac tgcattccgt 180
ttgttcccgc tgagatgggc acacacacag tcagcgtgaa gtacaagggc cagcacgtgc 240
ctgggagccc ctccagttc accgtggggc ccctagggga agggggagcc cacaagggtcc 300
gagctggggg ccctggcctg gagagagctg aagctggagt gccagccgaa ttcaagtatct 360
ggacccggga agctggtgct ggaggcctgg ccattgctgt cgagggcccc agcaaggctg 420
agatctcttt tgaggaccgc aaggacggct cctgtggtgt ggcttatgtg gtccaggagc 480
caggtgacta cgaagtctca gtcaagttca acgaggaaca cattcccagc agcccccttcg 540
tggtgcctgt ggcttctccg tctggcgacg cccgccgcct cactgtttct agccttcagg 600
agtcagggtc aaaggtcaac cagccagcct cttttgcagt cagcctgaac ggggccaagg 660
gggcgatcga tgccaagggtg cacagcccct caggagccct ggaggagtgc tatgtcacag 720
aaattgacca agataagtat gctgtgcgct tcatccctcg ggagaatggc gtttacctga 780
ttgacgtcaa gttcaacggc acccacatcc ctggaagccc cttcaagatc cgagttgggg 840
agcctgggca tggagggggc ccaggccttg tgtctgctta cggagcaggt ctggaaggcg 900
gtgtcacagg gaaccagct gagttcgtcg tgaacacgag caatgcggga gctgggtgcc 960
tgtcggtgac cattgacggc ccctccaagg tgaagatgga ttgccaggag tgccctgagg 1020
gctaccgcgt cacctatacc cccatggcac ctggcagcta cctcatctcc atcaagtacg 1080
gcggccccta ccacattggg ggcagcccct tcaaggccaa agtcacaggc ccccgctctc 1140
tcagcaacca cagcctccac gagacatcat cagtgtttgt agactctctg accaaggcca 1200
cctgtgcccc ccagcatggg nccccgggtc ctgggcctgc tgacgccagc aaggtggtgg 1260

```

```

ccaagggctg gggctgagca aggcctacgt aggccagaag agcagcttca cagtagactg 1320
cagcaaagca ggcaacaaca tgctgctggt gggggttcat ggccaagga cccctgcga 1380
ggagatcctg gtgaagcacg tgggcagccg gctctacagc gtgtcctacc tgctcaagga 1440
caagggggag tacacactgg tgggtcaaatg gggggagcag cacatcccag gcagccccta 1500
ccgcgttggt gtgccctgag tctggggccc gtgccagccg gcagccccc agcctgcccc 1560
gctacccaag cagcccgcgc ctcttcccct caaccccgcc ccaggccgcc ctggccgcc 1620
gcctgtcact gcagccgccc ctgccctgtg ccgtntctgc ctcacctgcc tcccagcca 1680
gccgtgacc tctcggttt cacttgggca gagggagcca tttggtggcg ctgcttgtct 1740
tctttggttc tgggaggggt gagggatggg ggtcctgtac acaaccaccc actagttctc 1800
ttctccagcc aagaggaata agttttgct tccattcwma aaaaaaaaaa aaaaaaaaaa 1860
tygggggggg kccgktaacc caattggcct ttaagnnggt ggtntta 1907

```

<210> 68

<211> 815

<212> DNA

<213> Homo sapiens

<400> 68

```

gggtcgaccc acgcgtccgt tttttttaag tgtgaatttt ttattgagat aaacaacagc 60
ataaagaata caagtagcca aatgggtttg aaaaaccaa ttaggtcaaa gttctaaatt 120
aaaaatagca gttgtgtttc aatttacctt attctagcaa ttwaagtwgg taacatacaa 180
atagttatwc tgatacaaga tattaaagac atactcagtt ttaatcaact acctctcaag 240
aaacagtagg gcctctgtaa aattggagac tgatagggtg atcagaaact caccctaaat 300
ctgaacgggt gccgtataa tttgtgacat ctggcaagat ttccctttat gtatatattt 360
taacaatccg cttggacacg aacaaagcca cacttctaac tgcttctggc gaactgattt 420
tatttttaat ttttttcaat aaagatattc ttagatactg aaagaaatag ttaatgagtt 480
tgcatttgtg cttgagaaaa tttggctcaa gtccatttgg ctgtagtgtc aacgatgttt 540
ccagtagtgt ttagatttgg tgtcttcaaa ggtagttgat taaaaccaag tgtgtcttta 600
atatcttgta tcagaataac tttgtatgtt accaacttaa attgctagaa taaggtaaat 660
tgatacacia ctgctatttt taatttagaa ctttgaccta atttgggttt tcaaaacat 720
tttggctact tgtattcttt atgctgttgt ttatttcaat aaaaaattca caccataaat 780
tatacttact aaaaaaaaaa aaaaaaaaaa actcg 815

```

<210> 69

<211> 1150

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (14)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (20)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (23)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (25)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1150)

<223> n equals a,t,g, or c

<400> 69

```

ctcgtgcaat tcgngcagan tgntnccctgg cctccttttg cttgcccgtg gctgttcctc 60
ctgggtcctc ttgccctggg ctggatgcct tcttcggctc cccctctgca tgtgataact 120
tggggtggcc cttggagctg tgccaaagct acacctcggg gtcctagtct caactggcct 180
gcgtactgct gtgggctcac cccgccttcc tcccacagcc ctgggcgctg cctatggcac 240
agccaagagc ggtaccggca ttgcggccat gtctgtcatg cggccggagc agatcatgaa 300
gtccatcatc ccagtggta tggctggcat catcgccatc tacggcctgg tgggtggcagt 360
cctcatcgcc aactccctga atgacgacat cagcctctac aagagcttcc tccagctggg 420
cgccggcctg agcgtgggcc tgagcggcct ggcagccggc ttgccatcg gcatcgtggg 480
ggacgctggc gtgcggggca ccgccagca gcccgaacta ttcgtgggca tgatcctgat 540
tctcatcttc gccgaggtgc tcggcctcta cggctctatc gtcgccctca tctctccac 600
aaagtagacc ctctccgagc ccaccagcca cagaatatta tgtaaagacc acccctcctc 660
attccagaac gaacagcctg acacatacgc acggggccgc cgccccagc agttggtctt 720
gtacatgcgc agtgtcctag tgcccatcgt ctgtttcccc ggccttgccc ccgccccccc 780
cgtgccgtgg acatctgggc cactcatcg cccctccagg cccccggcgc cccacccctc 840
agagtgtctc gtgtatgcgg atgatttaga attgtcattt ctctttactg gatgtttatt 900
tataaagatc tggcctgttc ctgctctgca ggagcggccc ttgtctccca gctatctata 960
accttagcta gagtgtcgcc ttgtgggttc ctgttgctga gacttcctgg atggagccgc 1020
cctcaccgcc gggcccgtgg cctgcgcgg agctgtgtcc aataaagttc ttggatgtga 1080
aaaaaaaaaa aaaaaaaaaa aaaaaaaraa aaaaaaaaaa aaaraaaraa aaaaaawaa 1140
gaaaaaaaaa                                     1150

```

<210> 70

<211> 344

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (287)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (333)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (339)

<223> n equals a,t,g, or c

<400> 70

```
cgcaggctct gcggccgggt tccttccgcg ggacggggag aaagagagag cgcgaaagag 60
agaggatgtc tctctcagat tggcacctgg cgggtgaagct ggctgaccag ccacttgccc 120
caaagtctat tctccagttg ccagagtcag agctgggtga atactctctg gggggctaca 180
gtatttcatt tctgaaacag ctcatctgctg gcaaaactoca ggagtcggtt ccagaccctg 240
agctgattga tctgatatac tgtggccgga agcttaaaga tgaccanacc ttgacttcta 300
cggatttcaa cctgggtcca catccatgtt ctncggaant cctg 344
```

<210> 71

<211> 448

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (425)

<223> n equals a,t,g, or c

<400> 71

```
tcgaccacag catccgaaga tgttcttget gccccttccg gctgccgggc gagtcgtcct 60
ccgacgtctg ggcgtgaaca gttctgggca cggggtctcg ccgccgcaga catgacgaag 120
ggtcttgttt taggaatcta tagtaaagac aaagaagatg atgtgccaca gtttacgagt 180
gcaggagaga atttcgataa attggtgtct ggaaagtga gagaaatttt gaacatatct 240
ggacctctc tgaaagcagg caaaacccga accttttatg gtctgcatga ggacttcccc 300
agcgtggttg tggtcggcct cggcagaaaag gcagctggag tcgatgacca ggaaaactgg 360
cmtgaaggca aagaaaacat cagagtcgcc atgcaacggg gtgcaggcag gttccaagac 420
ctggnaatct cttctgtgga aggtggat 448
```

<210> 72

<211> 2825

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1809)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2093)

<223> n equals a,t,g, or c

<400> 72

```
gagaaggagg tcgcgcggcc tcatcccggg ccgcgcccca ggccgcccgc ggccccgcgc 60
tcatgaggtt gctcgcgcgc cccgcgcgat cgccatggat cggatgaaga agatcaaacg 120
gcagctgtca atgacactcc gaggtggccg aggcataagac aagaccaatg gtgcccctga 180
gcagataggc ctggatgaga gtggtggtgg tggcggcagt gaccctggag aggccccac 240
```

```

acgtgctgct cctggggaac ttcgttctgc acggggccca ctcagctctg caccagagat 300
tgtgcacgag gacttgaaga tggggctctga tggggagagt gaccaggctt cagccacgtc 360
ctcggatgag gtgcagtctc cagtgaagat gcgtatgcgc aaccatcccc cagcaagat 420
ctccactgag gacatcaaca agcgcctatc actaccagct gacatccggc tgcctgaggg 480
ctacctggag aagctgaccc tcaatagccc catctttgac aagccctca gccgccgct 540
ccgtcgtgtc agcctatctg agattggctt tgggaaactg gagacctaca ttaagctgga 600
caaactgggc gaggggtacct atgccaccgt ctacaaaggc aaaagcaagc tcacagacaa 660
ccttgtggca ctcaaggaga tcagactgga acatgaagag ggggcaccct gcaccgccat 720
ccgggaagtg tccctgctca aggacctcaa acacgccaac atcgttacgc tacatgacat 780
tatccacacg gagaagtccc tcacccttgt ctttgagtac ctggacaagg acctgaagca 840
gtacctggat gactgtggga acatcatcaa catgcacaac gtgaaactgt tcctgttcca 900
gtgctccgt ggcctggcct actgccaccg gmagaagggt ctacaccgag acctcaagcc 960
ccagaacctg ctcatcaacg agaggggaga gctcaagctg gctgactttg gcctggccc 1020
agccaagtca atcccaacaa agacatactc caatgagggt gtgacctgt ggtaccggcc 1080
ccctgacatc ctgcttgggt ccacggacta ctccactcag attgacatgt ggggtgtggg 1140
ctgcatcttc tatgagatgg ccacaggccg tccccctttt ccgggctcca cgggtggagga 1200
acagctacac ttcactcttc gtatcttagg aaccccaact gaggagacgt ggccaggcat 1260
cctgtccaac gaggagttca agacatacaa ctacccaag taccgagccg aggccctttt 1320
gagccacgca ccccgacttg atagcgacgg ggcgcacctc ctcaccaagc tgttgacgtt 1380
tgagggtcga aatcggtatc ccgcagagga tgccatgaaa catccattct tcctcagtct 1440
gggggagcgg atccacaaac ttcctgacac tacttccata tttgactaa aggagattca 1500
gtacaaaaag gaggccagcc ttcggtcttc gtcgatgcct gactcaggca ggccagcttt 1560
ccgcgtggtg gacaccgagt tctaagccac agaccgaggc cccagcaggc agcggctgga 1620
gggatgccac acccctcaca gggcagcccc caactacatc ttccctgctt actctctgcc 1680
tacctgcctg agccatgttc acctgcccac ttgtccctg ctgcctgccc aaacacccca 1740
ccattggcct gtcaaccac ccattggcct gtctgctggg tgctaacaaa gctctcatca 1800
ctccttcant tgggtctgtct gtctctgtct tggtagttgc cggtaggacag catggccgtg 1860
ccagcctccc aactgaggc caggtctacc ccccatcata ccagcccma graccaytam 1920
cccacggsca gccaggggtc caragctagc ccaggctggg gatctcgact cagacaagat 1980
ggtgacaatg ccttgagtct gaggcacctc ctgcctgctt tcctgcctgc cccacctgcc 2040
tcatattgtg tgggcctttt tttgtttgtt tcatctattg ttttttttt ttnaattatt 2100
ttaaattgaga tttttgtttt ttttaaatgc aatatctctg tatacagact ggctgggccc 2160
acccctgcg tgtggccctc ccacagtatt ttgtgcaatg aagccctgct cccagccttt 2220
cagagacagg gacacagccc ctatttgaa ccctgatcat caccagacc tgggattggc 2280
tatgggaaaag catgccacag cactgcct tcctaccccc gcccgccatc cccagttgca 2340
gggggatctg gggactacca gagactctgg gaaatggaca aggtgggggg cccactctt 2400
tctctcctgc agtcccgtag ctggggcctc ctccctctc agggctctcc cagcccagtc 2460
cccttgcctc catcccactc ggtgctgttg ggtaggggcc ctgccaggaa ctgaccagct 2520
cagcgaggag ccataatgtg catatgtgca caagcagggt tgggggaggg ggggtgtgagg 2580
ggttgtgccc aggtgttgcc ccctatctcc tggggagggt gaggcagggc agggacagtc 2640
tccagggtca gtccctggat ggggtgttac ctcccttcc tccaccctaa gccctggggc 2700
cctgaaatgg ggtgggaggg caggggtggg agccctccta gtgggtttgg ggggttgggt 2760
tcctgaatgc accataatcg ctgtatgaaa tattaataag tctaaagtga aaaaaaaaaa 2820
aaaaa 2825

```

&lt;210&gt; 73

&lt;211&gt; 510

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 73

```

atgtacgaga gcgcattcaa agaacctagt agagaaaggt attctaacca ctgagaagca 60
gaatttccts ctatttgaca tgactactca tccagtgtacc aatacaacag agaaacagcg 120
actagtgaag aaacttcaag atagtgtact agagcgggtg gtaaatgacc ctgagcgat 180
ggacaagcga acactagcac tcctgggtgct agcccactcc tctgatgtgc tagagaatgt 240
cttctcctct ctgacagatg acaagtatga tgtggcaatg aatcgagcca aggacttagt 300
agaactggac cctgaagtgg aagggacaaa gccyagtgcc acagaratga tctgggctgt 360
gctggcagcc tttyaataaa tcytaaagcc rgyrggtggg tttctycttt tcccctgctg 420
gctggtgact gttcagagac mccwcaactga gttttgtgtg atgasatgtt ttccatcatt 480
ttttccttyc ttgaatcaga cttgtgaatt 510

```

<210> 74

<211> 458

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (382)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (388)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (424)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (448)

<223> n equals a,t,g, or c

<400> 74

```

gggtcgaccc acgcgtccgc tccacttaaa attcaacttc tgcttggttc atctgattct 60
ttcaaggtct taaatgttaa atgaaggggt aaaataggaa ggtatttaag taattagcag 120
gcctcctggg tcttgataac ttcagtgtct ctgggagctg cccggttggc caccagtctc 180
tgtggaatcc aggggcctct tcccaatatg gatttgacca gcacttcaat tagtgagttt 240
ccatkgacat cttagcatta ctctttaata cagacgcctt attttccagg gtttatgaaa 300
gtttaagtga caaccatgga ttgcaggaac agactgttga gaagctgttt ttccagtggg 360
aaagttgggt ccaggagatg angggagnc tgaatatagat cctgggatgg aaacataaag 420
tgngcagcca gattcccatc atgggctncc ccataaaa 458

```

<210> 75

<211> 377

<212> DNA

<213> Homo sapiens

<400> 75

```

gtcctggaaa cacatcaagc tcagctcctg tgtccagctc gcttctctgc tggactcctt 60
gatttttttt ttaatcattg ttgatttttg agcagtaacc aggctttttt ttccagatgt 120
tagtccacac ctattcatcc atggaccggc acgatggtgt. cccgagccac agctcgcggc 180
tctcccagct gggtcgggtg tcccaggagc cctactcgag cgccccgccc ctgtcccaca 240
ccccgtcgtc ggacttccag cgcgcctact tcccamcccc ctaccagccc ctccccctamc 300
amcagagcca ggacccctac tcccacgtca amgamcccta tccctgaacc cactgcacca 360
gccccagcaa catccct                                     377

```

<210> 76

<211> 2070

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (20)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (39)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (88)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2068)

<223> n equals a,t,g, or c

<400> 76

```

tcatgaatgg gaatcctggn cccaagaact ccgcttgcn g cagagggac ctgcagctga 60
ggacctatag cgttggtgcc atgacctnca gtgtatocca gggcaccgcc gtgtgtaata 120
taaagattgg ctgacaaaaa tgtcaggaaa acatgatgtt ggagcttaca tgctaata 180
taagggcgct aatcgtactg aaacagtcac gtcttttaga aaacgagaaa gttaaagtcc 240
tgctgatctc ttaaagcggg ccttcgtgag gatgagtaca agccctgagg ctttcctggc 300
gctccgctcc cacttcgcca gctctcacgc tctgatatgc atcagccact ggatcctcgg 360
gattggagac agacatctga acaactttat ggtggccatg gagactggcg gcgtgatcgg 420
gatcgacttt gggcatgcgt ttggatccgc tacacagttt ctgccagtcc ctgagttgat 480
gccttttcgg ctaactcgcc agtttatcaa tctgatgtta ccaatgaaag aaacgggcct 540
tatgtacagc atcatggtac acgcactccg ggccttcgc tcagaccctg gcctgctcac 600
caacaccatg gatgtgtttg tcaaggagcc ctctttgat tggaaaaatt ttgaacagaa 660
aatgtgaaa aaaggagggt catggattca agaaataaat gttgctgaaa aaaattggta 720
ccccgcagag aaaatatgtt acgctaagag aaagttagca ggtgccaatc cagcagtcac 780
tacttgatgat gagctactcc tgggtcatga gaaggcccct gccttcagag actatgtggc 840
tgtggcacga ggaagcaaag atcacaacat tcgtgcccaa gaaccagaga gtgggctttc 900
agaagagact caagtgaagt gcctgatgga ccaggcaaca gacccaaca tccttggcag 960
aacctgggaa ggatgggagc cctggatgtg aggtctgtgg gagtctgcag atagaaagca 1020

```

```

ttacattggt taaagaatct actatacttt ggttggcagc attccatgag ctgattttcc 1080
tgaacacta aagagaaatg tcttttgtgc tacagtttcg tagcatgagt ttaaatcaag 1140
attatgatga gtaaatgtgt atgggttaaa tcaaagataa gggtatagta acatcaaaga 1200
ttaggtgagg tttatagaaa gatagatatc caggcttacc aaagtattaa gtcaagaata 1260
taatatgtga tcagctttca aagcatttac aagtgtctgca agttagttaa acagctgtct 1320
ccgtaaatgg aggaaatgtg gggaaagcctt ggaatgccct tctgggtctg gcacattgga 1380
aagcacactc agaaggcttc atcaccaaga ttttgggaga gtaaagctaa gtatagttag 1440
tgtaacattg tagaagcagc ataggaacaa taagaacaat aggtaaagct ataattatgg 1500
cttatattta gaaatgactg catttgatat tttaggatat ttttctaggt tttttccttt 1560
cattttattc tcttctagtt ttgacatttt atgatagatt tgctctctag aaggaaacgt 1620
ctttatttag gagggcaaaa attttgggtca tagcattcac ttttgctatt ccaatctaca 1680
actggaagat acataaaaagt gctttgcatt gaatttggga taacttcaaa aatcccatgg 1740
ttgttgtagg ggatagtact aagcatttca gttccaggag aataaaagaa attcctatgt 1800
gaaatgaatt cctcatttgg aggaaaaaaa gcattgcatt tagcacaaca agatgaaatt 1860
atggaataca aaagtggctc cttcccatgt gcagtccctg tcccccccg ccagtccctc 1920
acacccaaac tgtttctgat tggcttttag ctttttgttg tttttttttt tccttctaac 1980
acttgatatt ggaggctctt ctgtgatttt gagaagtata ctcttgagtg ttttaataag 2040
tttttttcca aaaaaaaaaa aaaaaaantt 2070

```

<210> 77

<211> 997

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (619)

<223> n equals a,t,g, or c

<400> 77

```

ctcgccctcc tgactcttcc tgcagggtggc tcaggaagga ttcagcctgg ccacttggct 60
aggactctgc cagcacccat ctgagactga cctcttccgg gcctttggac actatgacct 120
tgatgctgcc cttcaggcag gaaacagggc tgggtgccttt tttcacctgc atggccagct 180
tccttccctg gcagtggaga gggcagccaa caggttctaa tgtcagagcc atcctttacc 240
agggtggcct gcttgtccct gtcttgccct ccacatcact ctactttttg gaaggccatg 300
gctgattaaa gaagtctctg tagtttccca agcaaagtgg aatctagaaa cagtgaaaaa 360
agttcagata actttgaatt gcattcaaga agtacacttc tttcccatg tccgtggctc 420
ttggagtctc cgtgatgcca ggctagagtc tgattatata ataattcaaa atggtaactc 480
ccaaggtaat gctttcttcc atttcatcag gttcttttat cccactgca cccctcccc 540
ttctcccttg cctatctgga tggcttctca gaagctcggc cctagtcctc cctgccttgg 600
cgggggccag agcccactna ctgctgaggc agcactgctc tcgtcagctg tgttgccctt 660
amccaagtgt cttcagaggg ttatgagtta gagtagctgg cctggggaga ggggtgcctc 720
ctgggtttga tctttagggt ctgactttct gcagagaaga tgttttacag atgtgtcaaa 780
gctgatgtaa tgtggttggg ggaggaaatc cagacccaaa gtgtttgtca gctgggtgta 840
caactgccta tgtgatcctc tgtcttaaaa tgatttctgt ctgtgctgcg aaacaaagac 900
aaggtagagt gttttctttt tttgtaataa tataaagctg tgtgtttctg attggatgat 960
tcactatgtg cattgttccy cctaagtgtc tttagta 997

```

<210> 78

<211> 1333

<212> DNA



<213> Homo sapiens

<220>

<221> misc feature

<222> (1254)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1297)

<223> n equals a,t,g, or c

<400> 78

```
gagaggagct gctgcgcgcc caggaagcgc cggggcaggc cgagccgccg gccgccgccg 60
aggtgcaggg ggctggcaac gaaaatgagc ctgcgcaggc cgacaagagc caccgcggagc 120
agcgcragct tcggcctcgg ctctgtacca tgaagaaggg cccagtggtc tatggcttca 180
acctgcacag cgacaagtcc aagccaggcc agttcatccg gtcagtggac ccagactccc 240
cggctgaggc ttcaggggctc cggggcccagg atcgcatgtt ggaggtgaac ggggtctgca 300
tggaggggaa gcagcatggg gacgtggtgt ccgccatcag ggctggcggg gacgagacca 360
agctgctggt ggtggacagg gaaactgacg agttcttcaa gaaatgcaga gtgatcccat 420
ctcaggagca cctgaatggt cccctgcctg tgcccttcac caatggggag atacagaagg 480
agaacagtcg tgaagccctg gcagaggcag ccttggagag cccagggcca gccctggtga 540
gatccgcctc cagtgcacac agcgaggagc tgaattccca agacagcccc caaaaacagg 600
actccacagc gccctcgtct acctcctcct ccgaccccat cctagacttc aacatctccc 660
tggccatggc caaagagagg gccaccaga aacgcagcag caaacgggcc ccgcagatgg 720
actggagcaa gaaaaacgaa ctcttcagca acctctgagc gccctgctgc caccagtgga 780
ctggcagggc cgagccagca ttccacccca ctttttcct tctccccaat tactcccctg 840
aatcaatgta caaatcagca cccacatccc tttcttgac aaatgatttt tctagagaac 900
tatgttcttc cctgacttta gggaaaggta atgtgttccc gtcctcccgc agtcagaaag 960
gagactctgc ctccctcctc ctactgagt gcctcatcct accgggtgtc cctttgccac 1020
cctgcctggg acatcgctgg aacctgcacc atgccaggat catgggacca ggcgagaggg 1080
caccctccct tcctccccc tgtgataaat gggccagggt ctgatcaaag aactytgact 1140
gcagaactgc cgytctyagt ggacagggca tytgttatga cagacctktg gcagacacgt 1200
cttgttttca ttgatttttg ttaagagtgc agtattgcag agtctagagg aatntatgtt 1260
tccttgatta acatgatttc ctggttggtta catccanggc aggcagtggc tcagctttaa 1320
atgtgttttc cta                                     1333
```

<210> 79

<211> 560

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (542)

<223> n equals a,t,g, or c

<400> 79

```
caatggggct gaggtgtgt ccactgaggc taagatgact gcctttcctg attggccttg 60
gcttttccat acattgtgtg acccttgccc tatgaccctt tggctgacct taccggaage 120
catgacgaca gcagcctttt gccattagac gcagggtgat ggtgaggatt ccaaggggta 180
```

```

gacaaaactg gttaatctga actaggtgac tgttaccttg cgtgttttgt ggccaaacca 240
ccaccaaaaa cctcacactg tgatgtaagt acttagtgta aaactagtaa acatttttgt 300
aaaatgtaga aatgcatgta atcagttaag ttttatattt tacaatgttc tgtaaaataa 360
aacttagcga ggtaaatcga ataaaggagc agtcactctc taacagattg taggagaggt 420
ttagttggat ttagtctatt tgacttgccc ttaatttaat tttatggcaa atcacaaatg 480
tgtcgaaggt ttagcaatat aatagcaaag tcctactcca gtaaataaaa gttggtatgt 540
tngtacttaa ctttcaaaag                                     560

```

<210> 80

<211> 3203

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1116)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1443)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1942)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3188)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3201)

<223> n equals a,t,g, or c

<400> 80

```

cggtagcgct gggtcgcggg cttcgggggt ctgcgctcgc ggctgcctgg actcagcagg 60
cccctggacc atgtcccgcg cctgcgggcc accgctcccg cctctctgct ttttcctttt 120
gttgctggcg gctgccgggtg ctcgggcccg gggatacgag acatgcccc aagtgcagcc 180
gaacatgctg aacgtgcacc tgctgcctca cacacatgat gacgtgggct ggctcaaaac 240
cgtggaccag tactttttatg gaatcaagaa tgacatccag cacgccgggtg tgcagtacat 300
cctggactcg gtcactctctg ccttgctggc agatcccacc cgtcgcttca tttacgtgga 360
gattgccttc ttctcccgtt ggtggcacca gcagacaaat gccacacagg aagtcgtgcg 420
agacctgtg cgccaggggc gcctggagtt cgccaatggt ggctgggtga tgaacgatga 480
ggcagccacc cactacgggtg ccatcgtgga ccagatgaca cttgggctgc gctttctgga 540
ggacacattt ggcaatgatg ggcgaccccc tgtggcctgg cacattgacc ctttcggcca 600
ctctcgggag caggcctcgc tgtttgcgca ratgggcttc gacggcttct tctttgggcg 660
ccttgattat caagataagt gggtagcgat gcagaagctg gagatggagc aggtgtggcg 720

```

```

ggccagcacc agcctgaagc ccccgaccgc ggacctcttc actggtgtgc ttcccaatgg 780
ttacaacccg ccaaggaatc tgtgtgtgga tgtgtgtgtg gtcgatcagc cgctggtgga 840
ggaccctcgc agccccgagt acaacgccaa ggagctgggtc gattacttcc taaatgtggc 900
cactgcccag ggccggtatt accgcaccaa ccacactgtg atgaccatgg gctcggactt 960
ccaatatgag aatgccaaaca tgtggttcaa gaaccttgac aagctcatcc rgctggtaaa 1020
tgcgcaaggc aaaaggaagc agtgtccatg ttctctactc ccccccgct tgttacctct 1080
gggagctgaa caaggccaac ctcacctggt cagtgnaaac tgacgacttc ttcccttacg 1140
cggatggccc ccaccagttc tggaccggtt acttttccag tcggccggcc ctcaaacgct 1200
acgagcgcct cagctacaac ttctctcagg tgtgcaacca gctggaggcg ctggtggggc 1260
tgcgggccaa cgtgggaccc tatggctccg gagacagtgc acccctcaat gaggcgatgg 1320
ctgtgtctca gcatcacgac gccgtcagcg gcacctcccg ccagcacgtg gccaacgact 1380
acgcgcgcga stttgcgga ggctgggggc ctgtcgaggt tcttctgagc aacgcctggc 1440
gcngetcaga ggcttcaaag atcacttcac cttttgcaa cagctaaaca tcagcatctg 1500
cccgtcagc cagacggcgg cgcgcttcca ggtcatcggt tataatcccc tggggcgga 1560
ggtgaattgg atggtacggc tgccggtcag cgaaggcggt ttctgtgtga aggacccaa 1620
tggcaggaca gtgcccagcg atgtggtaat atttcccagc tcagacagcc aggcgcaccc 1680
tccggagctg ctgttctcag cctcactgcc cgccctgggc ttcagcacct attcagtagc 1740
ccaggtgcct cgctggaagc cccaggcccc cgcaccacag cccatcccca gaagatcctg 1800
gtccctgct ttaaccatcg aaaatgagca catccgggca acgtttgatc ctgacacagg 1860
gctgttgatg gagattatga acatgaatca gcaactcctg ctgcctgttc gccagacctt 1920
cttctggtac aacgccagta tnagtgaca acgaaagtga ccaggcctca ggtgcctaca 1980
tcttcagacc caaccaacag aaaccgctgc ctgtgagccg ctgggctcag atccacctgg 2040
tgaagacacc cttggtgcag gaggtgcacc agaacttctc agcttggtgt tcccagggtg 2100
ttcgctgta cccaggacag cggcacctgg agctagagtg gtcggtgggg ccgatacttg 2160
tgggcgacac ctgggggaag gaggtcatca gccgttttga cacaccgctg gagacaaagg 2220
gacgcttcta cacagacagc aatggccggg agatcctgga gaggaggcgg gattatcgac 2280
ccacctggaa actgaaccag acggagcccc tggcaggaaa ctactatcca gtcaacaccc 2340
ggatttacat cacggatgga aacatgcagc tgactgtgct gactgaccgc tcccaggggg 2400
gcagcagcct gagagatggc tcgctggagc tcatggtgca ccgaagctgc tgaaggacga 2460
tggaagcgga gtatcgagc cactaatgga gaacgggtcg ggggcgtggg tgcgagggcg 2520
ccacctggtg ctgctggaca cagcccaggc tgcagccgcc ggacaccggc tcctggcgga 2580
gcaggaggtc ctggcccctc aggtggtgct ggccccgggt ggcggcgccg cctacaatct 2640
cggggctcct ccgcgcacgc agttctcagg gctgcgcagg gacctgccgc cctcggtgca 2700
cctgctcagc ctggccagct ggggccccga aatggtgctg ctgcgcttgg agcaccagtt 2760
tgccgtagga gaggattccg gacgtaacct gagcgcccc gttaccttga acttgaggga 2820
cctgttctcc accttcacca tcaccgcct gcaggagacc acgctggtgg ccaaccagct 2880
ccgcgaggca gcctccaggc tcaagtggac aacaaacaca ggccccacac cccaccaaac 2940
tccgtaccag ctggaccggg ccaacatcac gctggaaccc atggaaatcc gcactttcct 3000
ggcctcagtt caatggaagg aggtggatgg ttaggtctgc tgggatgggc cctccaagcc 3060
caagcctcct gctccggggg cagaccagac tctgactctc ctcttgggct gctgccatta 3120
aaacgctact actaagaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3180
aaatttanaa aaaaaaaaaa naa 3203

```

&lt;210&gt; 81

&lt;211&gt; 1710

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1424)

<223> n equals a,t,g, or c

<400> 81

```
aagagccgaa cggataagag aagaggaggg cgcgkatggc gtcggggcgc cccgaggagc 60
tgtgggaggg cgtggtgggg gccgctgagc gcttccgggc ccggactggc acggagctgg 120
tgctgctgac cgcggccccc ccgcaccacc ccgcccgggc ccctgtgcct atgctgcca 180
tggtcgagga gccctggcgg aggcagcgcg ccgttgccct caccacatcg cactggccca 240
cagggctgcc actgctgctc ggccctcctgc gccccacca gcaccacagc caccagtc 300
cacacccagc ccaccccggc ctaccctggc cagagaggac aacgaggagg acgaggatga 360
gcccacagag acagagacct ccggggagca gctgggcatt agtgataatg gagggctctt 420
tgtgatggat gaggacgcca ccctccagga ccttcccccc ttctgtgagt cagaccccca 480
gagtacagat gatggcagcc tgagcgagga gacccccgcc ggccccccca cctgetcagt 540
gccccagcc tcagccctac ccacacagca gtacgccaag tccctgcctg tgtctgtgcc 600
cgtytggggc ttcaaggaga agaggacaga ggcgcggtca tcagatgagg agaattgggc 660
gccctcttcg cccgacctgg accgcctcgc ggcgagcatg cgcgcgctgg tgctgcgaga 720
ggccgaggag acccagggtct tcggggacct gccacggccg cggcttaaca ccagcgactt 780
ccagaagctg aagcggaaat attgaagtcc agggaggagg cgcgccgggc cgcgtccgcc 840
ccgtcccaca ctacgcccc gccccactcc cggggcctgc taatctgagg ccgatccggg 900
accggcctcc ttgctctcc cattcccaag attgtccgc ctctgccaat cccgcgcgtc 960
cttccagccc acgacctgcc gcgcgagga ggggcwtctg tcccgtttcc cgattgggtc 1020
tgtcgtctct ctccgcctag cgacagattc cttctattaa gggattggct cgctgagttc 1080
taagctctaa atgggtcaac tcctttgttt tccgcctagc gacaagggat ttgctcgcac 1140
ggcattggct ccatcccta gtcgctggac agctcttttt ttgattggct caaatcctgt 1200
aaagggcttg accagtctct acatagtcac cgtccgcttt tcctgagttc tccctcccaa 1260
ttggctccag cttcctgggg gcgtggccaa gccctcctct tcccagaatt ggcccggggc 1320
cttcaattta cgttctttac actacgggga ctggggtcgt ctttgccac gtcccacaa 1380
cttgttccct gacccctca gggatggccc caaactgtcc ctgnccttg caccctttt 1440
cattggttcc atccatcccc acaacagcct gccaatcgaa gcccgccct gcacccagga 1500
tggtaccagc tcccgcctcc cgcctccac ctccacaggt gccttaaagg gccctcgta 1560
cccaaggtgg ggcaggggc cctcactctc cggccctggt gtgggggaga gaggagggg 1620
ttgggggatc ggcagttggg aggggcgctc tgagattaaa gatttttacc tctgagataa 1680
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1710
```

<210> 82

<211> 1379

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (280)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1365)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1378)

<223> n equals a,t,g, or c

<400> 82

```
aattcggcag agctgagccc cgggctgtgc agtccgacgc cgactgaggc acgagcgggt 60
gacgctgggc ctgcagcgcg gagcagaaaag cagaacccgc agagtccctc ctgctgctgt 120
gtggacgaca cgtgggcaca ggcagaagtg ggccctgtga ccagctgcac tggtttcgtg 180
gaaggaagct ccaggactgg cgggatgggc tcagcctgta tcaaagtcac caaatacttt 240
ctcttcctct tcaacttgat cttctttatc ctgggcgcac tgatcctggg cttcgggggtg 300
tggatcctgg ccgacaagag cagtttcacg tctgtcctgc aaacctcctc cagctcgtt 360
aggatggggg cctatgtctt catcggcgtg ggggcagtca ctatgctcat gggcttcctg 420
ggctgcatcg gcgcctgcaa cgargtccgc tgcctgctgg ggctgtamtt tgctttcctg 480
ctcctgatcc tcattgccc a rgtgacggcc ggggccctct tctacttcaa catgggcaag 540
gtaagcccc ctctccctcc ctcttcactg ggctggacca accatggggg tgattgactg 600
agtgtggggg atggacaagg aaccccccca gttgtcacag acagatccag taggtgtcag 660
ggacggcctc ctggacacta ttccttgtga atcaaatggg ggagcggttag aagagaaggc 720
ggcaggtgtr ggcagtcctc gctgggcctg gwtcttagcc tgacccccct gctttctagc 780
tgtgtggcct tgggcaagct gcttgccctt atgtgcctgt tccaccatct gtgaaaatgg 840
aaacaataag aaaactgaac tctcagagt gttgcaaaga ttattcgaga ttatctgagt 900
gaaacacata gcgcattggc ccataagtac tcaataaatg ttattcttgt tattattaag 960
rtacttttagc aactattaaa tccatgccac tcaccacaa atgaggttta gaaggagacc 1020
gttaataaaa acatcagtct tgtgtccgag gggagatgtt cagctttcag aaacagaaaa 1080
tcagacttac agcggcttaa agttgaaggc catctgtggt tgacttgacc ggaagtctgg 1140
tttgaagct cagaggccct ggttctggct gttgagcatc ctgctggga tggctttcct 1200
gcattatgac acttacctcg tggttccaag atggctgcca cagcaccagg cagatgtct 1260
gtgccgctgt ggcctgaaga tggggaagt ggcagtgcc gacatggcca tcccttttat 1320
ccagaaaagg cgcagtggct catgactgta atccccaata cttanggaag cagaagtng 1379
```

<210> 83

<211> 678

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (602)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (626)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (648)

<223> n equals a,t,g, or c

<400> 83

```
gcaagagcgg aagaaagcgg ctggtacccc ggaagcagtc gctgcaactt ccgggaggtg 60
cttgtgtgcc tgggtcgggg gctacggggc ccagggattg tgtttaaagt agtgcttcta 120
ccaacatgtc ccgtggttcc agcgcgggtt ttgaccgcca cattaccatt ttttcacccc 180
```

```

agggtcggct ctaccaagta gaatatgctt ttaaggctat taaccagggt ggccttacat 240
cagtagctgt cagagggaaa gactgtgcag taattgtcac acagaagaaa gtacctgaca 300
aattattgga ttccagcaca gtgactcact tattcaagat aactgaaaac attggttggtg 360
tgatgaccgg aatgacagct gacagcagat cccagggtaca gagggcacgc tatgaggcag 420
ctaactggaa atacaagtat ggctatgaga ttcctgtgga catgctgtgt aaaagaattg 480
ccgatatttc tcagggtctac acacagaatg ctgaaatgag gcctcttggt tgttgatga 540
ttttaattgg tatagatgaa gagcaaggcc ctcagggtata taagtgtgat cctgcagggt 600
antactgtgg ggtttaaac cactgnagcg ggagttaaac aaactggngt caaccagctt 660
ccttgaaaaa aaagtgga 678

```

<210> 84

<211> 2803

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (10)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (50)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (517)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (572)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1926)

<223> n equals a,t,g, or c

<400> 84

```

caacatgagn aatccttctc ctccctctgg ctggcttgga aatscaaaan ctcytcgcaa 60
cgtcccgcga raatctgggt gctctgccgg atggcatctc ggagctcttg attctcctcc 120
aggcarcgtc ggagggtctc aggagcgccc tgttctgaag gcagggtcag catggctggc 180
ttccccagag gagactcttc gccagtagc tcctgatctg ctgccgggcc accactgggc 240
tgcaccatct cacacagttg gctcttcag aggtgcctat tcatccaaca gggcaagggc 300
tgtcagcaga gtccgtcaga cgtgagaagg gtgggagcgg cggactgtga acgctggtag 360
ggccccggcg ctccgagaaa gtcccagttt cgcggtcgcc cttccctacc acgcttccgg 420
cttccggtgt catagctgtg ggatccggaa gtaaaaacac aagccccgcs cccrrgaact 480
cggggaagccg gcgakaagtg tgaggccgcg gtagggnccg atcccgtcc ggagagaagt 540
ctgagtcgcg cagctctgca ggcccgcgga antcgacagc gtcatggcag agcaggtggc 600

```

```

cctgagcccg acccaggtgt gcgggatcct gcgggaagag cttttccagg gcgatgcctt 660
ccatcagtcg gatacacaca tattcatcat catgggtgca tcgggtgacc tggccaagaa 720
gaagatctac cccaccatct ggtggctgtt ccgggatggc cttctgcccg aaaacacctt 780
catcgtgggc tatgcccgtt cccgcctcac agtggctgac atccgcaaac agagtgaacc 840
cttcttcaag gccaccccag aggagaagct caagctggag gacttctttg cccgcaactc 900
ctatgtggct ggccagtacg atgatgcagc ctctaccag cgcctcaaca gccacatgaa 960
tgccctccac ctgggggtcac aggccaaacc cctcttctac ctggccttgc ccccgaccgt 1020
ctacgaggcc gtcaccaaga acattcacga gtcctgcatg agccagatag gctggaaccg 1080
catcatcgtg gagaagccct tcgggagggg cctgcagagc tctgaccggc tgtccaacca 1140
catctcctcc ctgttccgtg aggaccagat ctaccgcacg gaccactacc tgggcaagga 1200
gatggtgcag aacctcatgg tgctgagatt tgccaacagg atcttcggcc ccatctggaa 1260
ccgggacaac atcgccctgc ttatcctcac ctcaaggag ccctttggca ctgagggtcg 1320
cgggggctat ttcgatgaat ttgggatcat ccgggacgtg atgcagaacc acctactgca 1380
gatgctgtgt ctggtggcca tggagaagcc cgccctccacc aactcagatg acgtccgtga 1440
tgagaaggtc aagggtgttg aatgcatctc agaggtgcag gccacaatg tggctcctgg 1500
ccagtacgtg gggaaccccg atggagaggg cgaggccacc aaaggggtacc tggacgacct 1560
cacggtgcc cgcggttcca ccaccgccac ttttgagcc gtgctcctct atgtggagaa 1620
tgagargtg gatgggtgc cttcatcct gcgctgcggc aaggccctga acgagcgcaa 1680
ggccgaggtg aggtgcagt tccatgatgt ggccggcgac atcttccacc agcagtgcaa 1740
gcgcaacgag ctggtgatcc gcgtgcagcc caacgaggcc gtgtacacca agatgatgac 1800
caagaagccg ggcatgttct tcaaccccga ggagtcggag ctggacctga cctacggcaa 1860
cagatacaag aacgtgaagc tccctgacgc ctacgagcgc ctcatcctgg acgtcttctg 1920
cggganccag atgcacttcg tgcgcaggac gagctccgtg aggcctggcg tattttcacc 1980
ccactgctgc accagattga gctggagaag cccaagccca tcccctatat ttatggcagc 2040
cgaggcccca cggaggcaga cgagctgatg aagagagtgg gtttccagta tgagggcacc 2100
tacaagtggg tgaaccccca caagctctga gccctgggca cccacctcca ccccgccac 2160
ggccaccctc cttcccgccg ccgaccccg agtcgggagg actccgggac cattgacctc 2220
agctgcacat tcctggcccc gggtcttgcc caccctggcc cgcccctcgc tgctgctact 2280
accgagccc agctacattc ctacgtgcc aagcactcga gaccatcctg gccctccag 2340
accctgcctg agcccaggag ctgagtcacc tccctcactc actccagccc aacagaagga 2400
aggaggagg cgccattcg tctgtcccag agcttattgg ccactgggtc tactcctga 2460
gtggggccag ggtgggagg agggacaagg gggaggaaag gggcgagcac ccacgtgaga 2520
gaatctgct gtggccttgc ccgccagcct cagtgccact tgacattcct tgtcaccagc 2580
aacatctcga gccccctgga tgtcccctgt cccaccaact ctgactcca tggccacccc 2640
gtgccacccg taggcagcct ctctgctata agaaaagcag acgcagcagc tgggaccctt 2700
cccaacctca atgccctgcc attaaatccg caaacagcca aaaaaaaaaa aaaaaaaaaa 2760
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aag 2803

```

&lt;210&gt; 85

&lt;211&gt; 1278

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 85

```

tcgacccacg cgtccgcaag aagctttttg agggcctgaa gttcttctctg aaccgagagt 60
gccccgtgag gccttgccct tcatcatcag gagtttttgt ggggaagtgt cctgggacaa 120
atctttgtgc attggggcca cctatgacgt cacagactcc cgcatacccc atcagattgt 180
cgaccggcct gggcagcaga cctcagtcac tggcaggtgc tacgtgcagc cccagtrrgt 240
gtttgactca gtgaacgcca ggctccttct ccccggtggca gactacttct ctgggggtgca 300
gctgccccca cacctttcac cctttgtgac cgagaaggaa ggagattacg ttccacctga 360
gaagctgaag ctgctggctc tgcagcgggg agaggaccca ggaaacctga atgagtcaga 420

```

```

agaggaggag gaagaggacg acaacaacga aggtgatggt gatgaagagg gagaaaatga 480
ggaggaggag gaagatgcag aggctggttc agaaaaggag gaagaggccc ggctggcagc 540
cctggaagag cagaggatgg aggggaagaa gcccagggtg atggcaggca ccttgaagct 600
ggaggataag cagcggctgg cccaggagga ggagagttag gccaaagcgc tggccattat 660
gatgatgaag aagcgggaga agtacctgta ccagaagatc atgtttggca agaggcgaaa 720
aatccgagag gccacaagc tggcggagaa gcggaagcc cacgatgagg cggtgaggtc 780
tgagaagaag gccagaagg caaggccgga gtgagtgcct ggggcccctc acagggctga 840
ggccagcccc tagcagctgg atgtggcaga ggcaggccag aggacctaa gtgatggac 900
cagagtcact tctcctcctc ctttctccag ccagccctga cccctcatgc tctctggctg 960
ggccagtggg cagccctcgc ttcccttgga tggagctgcc ctgctgggtg ctggtcagag 1020
aagaggcctc tgtgcccagc ctgattctct gctcccagga gccagtgaac tgaggtgacg 1080
aggcccaccc agccccctac ctactgcccc cattcatcct ggctttccac agccccctcc 1140
cacacagttg gacccgtgat tctcagggtg ctgtgatggg gtgagggtag ggggagcatt 1200
tgttattaaa tgactggact tttgtgccaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260
aaaaaaccca cgcgtccg                                     1278

```

<210> 86

<211> 2585

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2573)

<223> n equals a,t,g, or c

<400> 86

```

tcgaccacag cgtccgcggg ctatttggtg gagcccaagc ctggtgggtg gccttcaaga 60
accccgaggt gtcccctttg gctcgattcc caggaaactc ctcctcaacc ctttggcat 120
cagcattaca agccaaagcc tcaatccagg gccctttcgt actcctaaag cagggataag 180
gacctatcac ttccgctcca ccttgggcca gttccagggt ataattggga ggaagagagg 240
aaatgtggaa aagggtcgtg tggcaaagct gggaccagat ggtgcagctt tcctgcagat 300
tcccgagaa gagatccctg cctacatgtc tgtgcatoga ctcctgagga agctgctaag 360
tcgatatcgg cttccagtag caacccgaga gaacctgtt atcaatgact gctgcagagg 420
tgctatgctt tccctggcca caggctggcc cactctggaa gcgacctctc tctgttagtc 480
ccagaaattg aagatatgta cagcagcccc tatctgcgcc cctcagaatc tcctatcacc 540
gtcagaggtc actgcaccaa tccaggcacc agatattgct ggatgagtac tgggctctac 600
atacctggaa ggcaaattat agaagtctca ctgcctgaag ctgctgcctc tgccgacctg 660
aagatacaga ttggctgcca cacagatgac ctgaccaggg ccagcaagct tttccgaggc 720
ccactcgtaa ttaaccggtg ctgcttgagc aaaccacaa aatcgatcac gtgcctctgg 780
ggtggactcc tctatataat tgtgcctcag aacagcaaac tgggttctgt gcctgtcacc 840
gtgaaggggg ctgtgcatgc tccatactac aagctggggg agaccaccct ggaggagtgg 900
aagaggcgta tccaggagaa tccaggggccc tggggagagc tggccacgga caacatcatt 960
ctgaccgtgc cgaccgcaaa tcttcgtact ctggagaacc ctgagccgct gctccgcctc 1020
tgggatgagg tgatgcaggc tgtggcgaga ctgggagctg agcccttccc tttgcccctg 1080
cctcagagga ttgttgccga cgtgcagatc tcagtgggct ggatgcatgc agggtacccc 1140
atcatgtgcc atctggagtc agtcaggag atcatcaacg agaagctcat cagaaccaag 1200
gggtctgtgg gccccgtcca tgagctgggc cgcaaccagc agcggcagga gtgggagttc 1260
ccaccacaca ccaccgaggc camctgcaac ctgtggtgtg tgtatgtgca tgagacggtc 1320
ttgggcattc ctcgaagccg tgccaatatt gctctgtggc ccccagttcg ggagaagaga 1380
gtcagaatct acctgagcaa ggtcccaat gtgaaaaact ggaatgcatg gmccgcactg 1440

```



```

gaaacgtatt tacagctcca ggaagccttt ggttgggagc cattcatccg tctcttcacc 1500
gagtacagga accagaccaa cttgccca gaaaatggtg acaaatgaa tctgtgggtc 1560
aagatgttct cccaccaagt gcagaagaac ctggctccgt tctttgaggc ctgggctggc 1620
ccatccagaa ggaagtggct accagcctgg cctatctgcc tgaatggaag gaaaatatta 1680
tgaaattgta cctcctcaca cagatgcccc actgaaattg aagtcaagaa atgcaaaaag 1740
gaactgagca catctcagca aagaaaactg aagggatttg gttataagtg gagaggatct 1800
cagcatatct ctggaagata gaaagtggat gaagcatgat aatgaaagag tgaagaacct 1860
ttcagataaa atgtaagctg atctgaacaa cataacccca aagagacttg cgcacctgaa 1920
aagcttgtct actgaagaat tactccagtt gtaagattga gccctctcct actctcccc 1980
aactcttatg cacagaacac aggcagtctc cactattgat accagttaa aatttcttgt 2040
tattgttgct gttgttgttt gtataaagga attgaacagg ctgcttgca agagataaga 2100
gttggtgctc cagaaaaaaa tttctcttct agtggaata agtgccccct cccccagccg 2160
gtcagcta at tctctactga cagctgagac ctctactca agtgccctgt gccttcaggt 2220
atagaagagg tttcctgaag aaacagacct aactgtacaa cagcagagga aacccatgcc 2280
aactgttata caagttaaca gttatgttga ttcttaa atg gggaatggtg agttagaaat 2340
tcccagacat gggcgatggg gagggagag grataaggaa aagtcacgag gtaggawtta 2400
gggggccttg aaaatatgac aaactctgag gggaaacaaa grcmatktg gaaagawtaa 2460
cttaatttta attccatctc cagagagatt tgaggtgtat ttaagatgaa aaacaggata 2520
ctacaaagaa acgggaaaaac tcagggggtc aagaccagcc taggcaagat ggnaaaaaac 2580
cccc

```

&lt;210&gt; 87

&lt;211&gt; 385

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (385)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 87

```

gggtcgaccc acgcgtccgc atgaatttgt cacaatctta tcaataatca ttactctgtt 60
ttttatattt caactaaaag tatcaaaata tagctttcca gaaaaccccg aaccaaagtc 120
actgactaca tcaaagtcta ctacaccttg agaaaacaaa tgaacgaaa tctattttcc 180
tcattcatta cccaacaat aataggactc cctatcgtaa ttattatcac tatgtttcca 240
agcattatat tcccatcacc taccgactr aatcaataat cgactscatc tccattccaa 300
caatgattag tgcactgaac atscaaaaca aatrttgatc catgccacaa ccaaaaagga 360
caaactggag cccggatatt gatan

```

385

&lt;210&gt; 88

&lt;211&gt; 2500

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (429)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

<221> misc feature  
<222> (1088)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2480)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2482)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2491)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2497)  
<223> n equals a,t,g, or c

<400> 88  
tcgacccacg cgtccgcccc cgcgtccgctc tccaccgctg ctgccgccgc cctggccgcc 60  
gccgcagtgaa agctaagca cttggctgct gttgaggaaa ggaagatcaa atctttggtg 120  
gcccgtgctgg tggagaccca gatgaaaaag ttggagatca aacttcggca ctttgaggag 180  
ctggagacta tcatggaccg ggagcragaa gcactggagt atcagaggca gcagctcctg 240  
gccgacagac aagccttcca catggagcag ctgaagtatg cggagatgag ggctcggcag 300  
cagcacttcc aacagatgca ccaacagcag cagcagccac caccagccct gccccaggc 360  
tcccagccta tcccccaac aggggctgct gggccaccgc caktccatgg cttggctgtg 420  
gtctccagct ctgtagtccc tgctcctgct ggagtgaggg cccctccagg aagtttgagg 480  
ccttctgaac agattgggca ggcagggtca actgcagggc cacagcagca gcaaccagct 540  
ggagcccccc agcctggggc agtcccacca ggggttcccc cccctggacc ccatggcccc 600  
tcaccgttcc ccaaccaaca aactcctccc tcaatgatgc caggggcagt gccaggcagc 660  
gggcacccag gcgtggcggg taatgctcct ttgggtttgc cttttggcat gccgcctcct 720  
cctcctcctc ctgtccatc catcatcca tttggtagtc tagctgactc catcagtatt 780  
aacctccccg ctctcctaa cctgcatggg catcaccacc atctcccgtt cgcgccgggc 840  
actctcccc cactaacct gcctgtgtcc atggcgaaac ctctacatcc taacctgcg 900  
gcgaccacca ccagccatc ttccttgccct ctccggccgg ggctcggatc cgcgcagcc 960  
caaagccctg ccattgtggc agctgttcag ggcaacctcc tgcccagtgc cagccactg 1020  
ccagaccacg gcacccccct gcctccagac cccacagccc cgagccccag gcacgggtcac 1080  
ccctgtgncc acctccacag tgaggagcca gccagacatc tctccccctc acccctgtg 1140  
gacatcacgg ttccaggaa agccttccc ccaccactgg gaccctcccc agcctggaga 1200  
gttcatcact acgtaaggaa agctccttcc gcccctccaa agccctcacc atgcctaaca 1260  
gaggcatgca tttttatatc agattattca aggacttctg tttaaaagat gtttataatg 1320  
tctgggagag aggataggat ggggaatgctg ccctaaagga agggctgggtg aaaggtgttt 1380  
atacaagggt ctattaacca cttctaaggg tacacctccc tccaaactac tgcattttct 1440  
atggattaaa aaaaaaaaaa aaagtagatt ttaaaaagcc acattggagc tcccttctac 1500  
ccactaaaaa ataaccaatt ttacatttt ttgaggggga gtgagtttta ggaaagggga 1560

```

attaagattc cagggagagc tctggggata gaacagggcg cagattccat ctctcccaa 1620
gccccttttt agtgactaag tcaaggcccc aactcccctc cccacccta cgctgagctt 1680
attcgagttc attcgacta ataatccctc ctgcggcttc ctcatgttg ctgttttagg 1740
ccacccagc tcagccaatg attcctttcc ctctgaatgt cagttttgtt tttaaaagtc 1800
acttgcttag ttgatgtcag cgtatgtgta tttggggggg aaaacctaat ttcgggggatt 1860
tctgtggtag gtaataggag aagaaagggc actgggggct gttctccttc cttccctggg 1920
ctgtatccat ggactcctgg aaggcacaga gaaggagct ataaggaggat gtgaagtttt 1980
aaaacctgaa attgtttttt aaagcactta agcacctcca tattatgact tggggggtca 2040
ccccttagct tcctccctct cccaccaaga ctatgagaac ttcagctgat agctgggggc 2100
tcccagatg aggatgcagg gatttgggag cagtgggaaga gggtgcccaa ccttggggtg 2160
gaccaaccct tggctcgag ctcaactctg cttcccgcat tcctgctcca cgtgtcccag 2220
cttctcccct gtgacgggaa ggcagggtgt actccaggct ctgcactggg tcttcttggg 2280
tcctcccacc aggcctttt ttctcatgt ccccatgttt ctctccctct gcgtcttagc 2340
acctttcttc tgttcaaagt tttctgtaa ttttctctt ttttcttct tttttttt 2400
tttttttata aattaatttg ctttcagttc caaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2460
aaaaaaaaaa aaaaaaaaaa tngagggggg ncccgnacc 2500

```

<210> 89

<211> 1409

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (841)

<223> n equals a,t,g, or c

<400> 89

```

aggagtatgt atttcccgcc aagaagaagc tgcaggaata ccgggtctta attaccaccc 60
tcatcactgc cggcagttgg tctcgcccca gtttcccatt gatcacttca cacacatctt 120
catcgatgag gctggccact gcatggagcc tgagaagtct ggtagctata gcagggtga 180
tggaagtaaa ggaacacaggt gatccaggag ggcagctggt gctggcagga gaccctcggc 240
agctggggcc tgtgctgctg tccccactga cccagaagca tggactggga tactcactgc 300
tggarcggtc gctcacctac aactccctgt acaagaaggc ccctgatggc tatgacccc 360
agttcataac caagctgctc cgcaactaca ggtctcatcc caccatcctg gacattccta 420
accagctcta ttatgaaggg gagctgcagg cctgtgctga tgtcgtggat cgagaacgct 480
tctgccgctg ggcggsccta cctcgacagg gctttcccat catctttcac ggcgtaatgg 540
gcaaagatga gcgtgaaggc aacagcccat ccttcttcaa ccctgaagag gctgccacag 600
tgacttccta cctgaagctg ctctggcccc cctcctccaa gaagggcaaa gctcgctga 660
gccctcgaag tgtgggcgtc atctccccgt accggaaaca ggtggagaaa atccgttact 720
gcatcaccaa acttgacagg gagcttcgag gactggatga catcaaggac ttgaagggtg 780
gttcagtaga agaattccaa ggccaagaac gaagcgtcat cctcatctcc accgtgcgaa 840
nagccagagc tttgtgcagc tggatctgga ctttaatctg ggtttcctta agaaccctaa 900
gaggttcaat gtagctgtga cccgggccaa ggcctgctca tcatcgtggg gaacccctt 960
ctcctgggcc atgaccctga ctggaaagta ttcctggagt tctgtaaaga aaacggaggg 1020
tataccgggt gtcccttccc tgccaaactg gacctgaac agggacagaa tttactgcaa 1080
ggctctgagca agctcagccc ctctacctca gggeccca gycatgacta cctccccag 1140
gagcgggagg gtgaaggggg cctgtctctg caagtggagc cagagtggag gaatgagctc 1200
tgaagacaca gcacccagcc ttctcgcacc agccaagcct taactgcctg cctgaccctg 1260
aaccagaacc cagctgaact gccctccaa gggacaggaa ggctggggga gggagtttac 1320
aaccgaagcc attycaccck cctccctgct ggggagaatg acacatcaag ctgctaacia 1380

```

ttgggggaag gggaaggaag aaaactctg

1409

&lt;210&gt; 90

&lt;211&gt; 1336

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (49)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1284)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1317)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1333)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 90

agaacagtac ctccctctca ctgaggaaga actagaaaaa gaagcaaana aagttgaagg 60  
at ttgatctg gttcagaagc caagttatta tgtagactg ggatccctgt ctaccaagct 120  
tactcccgt gcctaccagc aggctctcag cagggttaaa gaagctaagc aaaaaagcca 180  
acagaccatt tctcagctcc attctactgt tcacctgatt gaatttgcca ggaagaatgt 240  
gtatagtgcc aatcagaaaa ttcaggatgc tcaggataag ctctacctct catgggtaga 300  
gtggaaaagg agcattggat atgatgatac tgatgagtc cactgtgctg agcacattga 360  
gtcacgtact cttgcaattg ccgcgaacct gactcagcag ctccagacca cgtgccacac 420  
cctcctgtcc aacatccaag gtgtaccaca gaacatccaa gatcaagcca agcacatggg 480  
ggtgatggca ggcgacatct actcagtgtt ccgcaatgct gcctccttta aagaagtgtc 540  
tgacagcctc ctcaattcta gcaaggggca gctgcagaaa atgaaggaat ctttagatga 600  
cgtgatggat tatcttgta acaacacgcc cctcaactgg ctggtaggtc ccttttatcc 660  
tcagctgact gagtctcaga atgctcagga ccaagggtgca gagatggaca agagcagcca 720  
ggagaccag cgatctgagc ataaaaactca ttaaacctgc ccctatcact agtgcatgct 780  
gtggccagac agatgacacc ttttgttatg ttgaaattaa cttgctaggc aaccctaaat 840  
tggaagcaa gtagctagta taaaggccct caattgtagt tgtttccagc tgaattaaaga 900  
gctttaaagt ttctggcatt agcagatgat ttctgttcac ctggtaagaa aagaatgata 960  
ggcttgtcag agcctatagc cagaactcag aaaaaattca aatgcactta tgttctcatt 1020  
ctatggccat tgtgttgccct ctgttactgt ttgtattgaa taaaaacatc ttcattgtgg 1080  
ctggggtaga aactggtgtc tgctctggtg tgatctgaaa aggcgtcttc actgctttat 1140  
ctcatgatgc ttgcttgtaa aacttgattt tagtttttca tttctcaaat aggaatacta 1200  
cctttgaatt caataaaatt cactgcagga tagaccagtt aaaaaaaaaa aaaaaaaaaa 1260  
aaaagggggg ccgcccaagg grtncccccg agggggggccc cagctttacg cgtggcntgc 1320  
gacgtccaaa gcnccc 1336

<210> 91  
<211> 787  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (677)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (725)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (742)  
<223> n equals a,t,g, or c

<400> 91  
ggcacgagct gtggggctgt gggcctgtta cccccaggcg cacagctccc tccggctggg 60  
cccaggctcc actcagtac acggctcaag tctacatgga gctgcagggc ctggtggacc 120  
cgcagatcca gctacctctg ttagccgccc gaagtacaag ttgcagaagc agcttgatag 180  
cctcacagcc aggaccccat cagaagggga ggcagggact cagaggcaac aaaagctttc 240  
ttccctccag ctggaattgt caaaactgga caaggcagcc tctcacctcc rgcagctgat 300  
ggatgagcct ccagcccag ggagcccgga gctctaactc atcatcccca tcagttttcc 360  
tccctctcag acctgtcttt gaggacaaaac agatttgtca gctgtcaggg tgcagtggga 420  
cgtcagagac tatgtgttcc atcgccctca ttgtgtaaat gaggacacag actggcttgg 480  
tcgcagtac tgtggtgtcc ttgagatgct cacattactg cccggcctgc ctcccacctg 540  
gaagtctggg aatgaggaga ttgagataaa cttttgaaat cccaaacatg tctgtttatg 600  
gctcttttgt ccccttttgt cccagtgggt acttttgtgc ttctgagttg tcccctgaga 660  
gcttggtctg ggaaaanagg aaggaagggg tcctcactgg aggaagagga acctttctaa 720  
gtcangggta aggggaatgg gnacagttgg ttcccgggtc taacctcctt ttctggactg 780  
acaagtg 787

<210> 92  
<211> 1657  
<212> DNA  
<213> Homo sapiens

<400> 92  
cgcgctccgcc cacgcgtccg cccacgcgtc cggctactca gaggaagggg cggttggtgc 60  
ggcctccatt gttcgtgttt taaggcgcca tgagggtgga cagaggccgt ggtcgtggtg 120  
ggcgctttgg ttccagagga ggcccaggag gagggttcag gccctttgta ccacatatcc 180  
catttgactt ctatttgtgt gaaatggcct ttccccgggt caagccagca cctgatgaaa 240  
cttccttcag tgaggccttg ctgaagagga atcaggacct ggctcccaat tctgctgaac 300  
aggcatctat cctttctctg gtgacaaaaa taaacaatgt gattgataat ctgattgtgg 360  
ctccagggac atttgaagtg caaattgaag aagttcgaca ggtgggatcc tataaaaagg 420  
ggacaatgac tacaggacac aatgtggctg acctggtggt gatactcaag attctgccaa 480

```

cgttggaagc tgttgctgcc ctggggaaca aagtcgtgga aagcctaaga gcacaggatc 540
cttctgaagt ttttaaccatg ctgaccaacg aaactggcct tgaaatcagt tcttctgatg 600
ctacagtga gattctcatt acaacagtgc cacccaatct tcgaaaactg gatccagaac 660
tccatttgga tatcaaagta ttgcagagtg ccttagcagc catccgacat gcccgctggt 720
tcgaggaaaa tgcttctcag tccacagtta aagttctcat cagactactg aaggacttga 780
ggattcgttt tcctggcttt gagccctca caccctggat ccttgacctg ctaggccatt 840
atgctgtgat gaacaacccc accagacagc ctttgcccct aaacgttgca tacaggcgct 900
gcttgagat tctggctgca ggactgttcc tgccagggtc agtgggtatc actgaccct 960
gtgagagtgg caactttaga gtacacacag tcatgacctt agaacagcag gacatggtct 1020
gctatacagc tcagactctc gtccgaatcc tctcacatgg tggctttagg aagatccttg 1080
gccaggaggg tgatgccagc tatcttgctt ctgaaatata tacctgggat ggagtatag 1140
taacaccttc agaaaaggct tatgagaagc caccagagaa gaaggaagga gaggaagaag 1200
aggagaatac agaagaacca cctcaaggag aggaagaaga aagcatggaa actcaggagt 1260
gacattccct tcaactcctt tcctacccaa gggggaagac tggagcctaa gctgcctgct 1320
actgggcttt acatgggtgac agacatttcc gtgggatagg gaagatagca ggaagaaaag 1380
taaactccat agaagtgtca ttccactggg ttttgatatt ggcttagctg ccagtctccc 1440
atgtgtgacc tatgccatcc atctataatg gaggatacca acatttcttc ctaatatctc 1500
ataatctcca actcctgaaa acccctctct caactaatac tttgctgttg aaatgttgtg 1560
aaatgttaag tgtctggaag tttttttt taagaaaaac tattaagta cttcctagta 1620
ggaaaaaaaa aaaaaaaaaa aaacycgggg gttttct 1657

```

<210> 93

<211> 485

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (478)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (485)

<223> n equals a,t,g, or c

<400> 93

```

aattcggcac gaggggttct gcactaacag cctccaagcc ccctggcact tcttttgccc 60
tgagagtgtc ccaggggatt cagagtctcc agaaagatat ggctrggcca actctgttgc 120
ctacctrgcc tgaccagtc ggagcctgac atggtggagg gaaagggaga caagtggggc 180
tgactcggg ccagaggcca gctaggagg aaaccgcagc ttcctggggc ttgtgtgtga 240
agattcctga cttagggggt gcttttgttt acaagatgca agaggggaaa cctgtccccc 300
actcatcgag acaacatgcc cagttatcag ggagtcctgt gtcacaaggt ctgtctctgc 360
cattgtaagc aagtgccttg ggcgagctgg cctctgcccc acagtctcat ctgtacaccg 420
acagggttga tgctccctc acagggttga gaacaagagc cakttggcc attaaaaana 480
aaaaan

```

<210> 94

<211> 764

<212> DNA

<213> Homo sapiens

<220>  
<221> misc feature  
<222> (202)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (565)  
<223> n equals a,t,g, or c

<400> 94  
ccccagccag tctgccctct gccatggggg gcggagagga cgaggaggag gccaccgact 60  
atggagggac ctcagtgccg actgccgggg aggccgtgcg ggggctagaa acagctctgc 120  
grtggttgga gaaccaggac ccagagaggg tggggccact gaggttggtg cagttgcgct 180  
cactcatcag catggcccg angctggggg gcacgcggca taccacagca ggcccctatg 240  
acggtgtgtg accaggccas ccagtgacc tttctcctgc tgcacttgga gggaggggac 300  
atacacacag tctcccatct ctctccct cccctggggg tggcccaccg catgggtaca 360  
gggggttcca ggaatccaaa tccagcatgg cttggaggag ctctgttggt gagaggtcgc 420  
cctgcctcac tggcaccctg ggggcacagc tggaaagagag gcctggccca tgctcctctc 480  
agggcaggca catgtacggg gcatacaagg cacagcgctt gttggaacag gtggctgtgt 540  
tctgtctctg gccccgtgc ggctngcctc cggccctgca ccagtcacat gcaactggacg 600  
agggccgaaa ctctgtctg ctatcgagcc ctggtgctat gtggcccccg agccacagca 660  
caatcatctc agtggcgaag cacaccactt gattctatatt ttttttaaca cattaaatct 720  
gtttttaaag ataaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 764

<210> 95  
<211> 707  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (45)  
<223> n equals a,t,g, or c

<400> 95  
atttaggtga cactatagaa ggtacgcctg caggtaccgt tccgnaattc ccgggtcgac 60  
ccacgcgtgc catcatggcg caggatcaag gtgaaaagga gaaccccatg cgggaacttc 120  
gcatccgcaa actctgtctc aacatctgtg ttggggagag tggagacaga ctgacgcgag 180  
cagccaaggt gttggagcag ctacagggc agaccctgt gttttccaaa gctagataca 240  
ctgtcagatc ctttggcatc cggagaaatg aaaagattgc tgtccactgc acagttcgag 300  
gggccaaggc agaagaaatc ttggagaagg gtctaaaggt gcgggagtat gagttaagaa 360  
aaaacaactt ctcatatact ggaaactttg gttttgggat ccaggaacac atcgatctgg 420  
gtatcaaata tgacccaagc attggtatct acggcctgga cttctatgtg gtgctgggta 480  
ggccagggtt cagcatcgca gacaagaagc gcaggacagg ctgcattggg gccaaacaca 540  
gaatcagcaa agaggaggcc atgcgctggt tccagcagaa gtatgatggg atcatccttc 600  
ctggcgaata aattcccgtt tctatccaaa agagcaataa aaagttttca gtgaaaaaaa 660  
aaaaaaaaa aaaaaaaggg ggcccccttt tgggggtccc ctggggg 707

<210> 96

<211> 815  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (16)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (45)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (50)  
 <223> n equals a,t,g, or c

<400> 96  
 aacccccctac tccctnccgt aattttttgta agcccttaaa ataanaaatn aaaaatycca 60  
 taacccccaa agaagaatcc cccccacatt waggccttggt aagtaaatgc ctcttgaccc 120  
 caagcccgaa gatgcccccc attctctwag tgatggcggc gttaggggtt gagagaagg 180  
 aatttggctc aacttcagtt gagaggggtgc agtccagaca gcttgactgc ttttaaatga 240  
 ccaaagatga cctgtggtaa gcaacctggg catcttagga agcagtcctt ggagaaggca 300  
 tgttcccaga aaggtctctg gagggacaaa ctactcagt aaaacataat gtatcatcat 360  
 gaagaaaact gattctctat gacatgaaat gaaaatttta atgcattggt ataattacta 420  
 atgtacgctg ctgcaggaca ttaataaagt tgctttttta ggctacagtg tctcgatgcc 480  
 ataatcagaa cacacttttt ttctcttttc tcccagcttc aaatgcaaat tcatcattgg 540  
 gctcactttc aataactgca gtgtttcccg ccttgggctt gcagcagaaa aacctgacaa 600  
 catagtgttt gctaaggcag taatttagac ttaccttat ttgtgattac tgtagtgtatt 660  
 gattgattga ttactattaa ctacaaggta taatttacta tcaccttatt taaattttat 720  
 gaattaattt gaatgttttt tacactaact aacttttccc aataaagtcc actatgaaac 780  
 cactgacaaa aaaaaaaaaa aaaaaaaaaa aaaaa 815

<210> 97  
 <211> 658  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (627)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (634)  
 <223> n equals a,t,g, or c

<220>



<221> misc feature  
<222> (635)  
<223> n equals a,t,g, or c

<400> 97  
catcattggc gcggggctgt cagcggccgg acgcggtcct ctacgcccg cactacaaca 60  
tcccgggtgat ccatgccttc cgccggggccg tggacgaccc tggcctggtg ttcaaccagc 120  
tgcccaagat gctgtacccc gagtaccaca aggtgcacca gatgatgcgg gagcagtcca 180  
tcctgtcgcc cagcccctat gagggttacc gcagcctccc caggcaccag ctgctgtgct 240  
tcaaggaaga ctgccaggcc gtgttccagg acctcgaggg tgtcgagaag gtgtttgggg 300  
tctccctggt gctggtcctc atcggctccc accccgacct ctccctcctg cctggggcag 360  
gggctgactt tgcagtggat cctgaccagc cgctgagcgc caagaggaaac cccattgacg 420  
tggacccctt cacctaccag agcaccgcc agraggccct gtacgccatg gggccgytg 480  
ccggggacaa cttcgtgagg tttgtgcagg ggggcgcctt ggctgtkgcc agctccctgc 540  
taaggaagga acagaaccac ctacatcgcc aacctggtc cagcctraga ggaatacatc 600  
ctctgatcga cctcaaatcc ggagttncct cttnncttgt caaattgacc gcccaata 658

<210> 98  
<211> 249  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (248)  
<223> n equals a,t,g, or c

<400> 98  
aaaatggtag acctgacagt accggtccgg caattcccgg gatattgagc tggggttttg 60  
agactscctt tagagataga gaaacagacc caagaaatgt gctcaattgc aatggggccac 120  
atacctagat ctccagatgt catttcccct ctcttatttt aagttatgtt aagattacta 180  
aaacaataaa agctcctaaa aaatcaaaaa aaaaaaaaaa aaaaaaaaaa aacccccggg 240  
ggggcccng 249

<210> 99  
<211> 752  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (612)  
<223> n equals a,t,g, or c

<400> 99  
acggcttcaa ccgcagcttc tgcggccgca acgccacggt ctacgggaag ggcgtgtatt 60  
tcgccaggcg cgctccctg tcggtgcagg accgctactc gcccccaac gccgatggc 120  
ataagcggtt gttcgtggca cgggtgctga ctggcgacta cgggcagggc cgccgcggtc 180  
tgcgggcgcc cctctgcgg ggtcctggcc acgtgctcct gcgtacgac agcgcctgtg 240  
actgcatctg ccagcccagc atcttcgtca tcttccacga caccagggc ctgcccaccc 300  
acctcatcac ctgcgargca cgtgccccgc gttcccccg acgacccctc tgggtctccc 360

```

ggccgctccc cagacactta accgaagggg ccaccctctg gcctcctgct tcccaggetc 420
ccagctccgc acaggctgat gctccccgcc cccaactgtg gccgcctgag ctgtccccgg 480
ggasgccctg cctccctctg cgggctccag aaggcgggtgt gggggatggc ggtcagcagc 540
ggccgagggg ggccgggcta ggtcccagcc tgggcccagc ccaccaccag gggtcagcag 600
agcccaggag gngacaccgy ccgcccgcg ctcccagacc tcgcccagat cggctctgtt 660
gtttgaataa acgtgaacgt gaacccaggc ggaagggacc cgggaaaaaa aaaaaaaaaa 720
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa                                     752

```

<210> 100

<211> 3059

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (14)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (28)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (109)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3019)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3047)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3058)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3059)

<223> n equals a,t,g, or c

<400> 100

```

ggggtaaaac ccngaaaaa aactccanat tttaattaaa tggcctcctc cttccccccc 60
ttctttcccc cgtccccca actcccttc ctcgtctctt tccccccnc cctctccct 120

```

tttctcccca tctttcacct tcctaatttc agtgaaattg gagcgatttg aaattccaat 180  
caaggttcga ttaagcccag agccatggac ccctgaaact ggtttggtta ctgatgcttt 240  
caaactgaaa aggaaggagc tgaggaacca ttacctcaaa gacattgaac gaatgtatgg 300  
gggcaataaa aatgttggtg tcttattgac agttgtgcag gaggtagcct ggtggttttc 360  
aacctctaga attttaagcc ttgttgtaac tgtagaatg taaggatat cattctaaag 420  
atagagtaaa aagaaaacaa aacccaaagt tattaataat gttgtccggt ttactttaac 480  
ttagttttgc atagttctag tgcagctgaa attgaaaagt tatttccctt tagctgtgtt 540  
attatagagc agaaattctg tttttaaaaa ttagcctaag atatacttgt ttttgtaaag 600  
aaaaatattt aatgttgaaac aaaataaatt ggagttggag tagaatgtag tttgaggaaa 660  
tttgagcgtt ccaatgcctc ttgtcttcct atttcagaag tttaaattt aagcatgaca 720  
gaaaatatgt attaacacta ctcaaagcaa aagtgtgca gggctttaaa attctcttcc 780  
aaccatttat cttgaaggaa aaattcaata gtaataaat acmcaaaatc aaataatacc 840  
ttagaaggta ttaagattat aattgttgca taggttagat atagagtcac tgtaatgttg 900  
tgaataatta cagtgcctaa aataagaata gaacaacata tacaacacca aaaaatatct 960  
agtaatatat ttaaagggaag attgagctgc ttttttgtaa actttgagat ctaaaaataa 1020  
ctgtaattat ttgaatgact aagaggaaag tacatttttt gaaatgctga aaattgcctt 1080  
tctgtgttta ttcaaacctga aaagctgaga ccaagagcaa ggaaggtaaa aagttaacag 1140  
gcaaactatt tctcttagaa aaggtgataa aatcataagt atttgaatt agaacccttk 1200  
cacagcactg aacctgggaa agagatttaa actctgaatt tatctttgat aacagggtat 1260  
gatttttaaaa tgtacatgta ttaaattaca ttgttaattt aaggtctgtt tgctgttgct 1320  
gattttattc ttgatcagta gtttgcatth cagaaagcct ttcattttgc ttttaatttta 1380  
gcaaagcggg ttataatgaa tgacttcccc aatatcttgc ttgaacttac aggtgattaa 1440  
cttgatgag ttttggaag ttaaaggga gaaaacactg ttatcatttt ttcctgtttg 1500  
ggaagagctt agaaactgga aatactagat ttgggagaag ggcagagtta cttgataagg 1560  
gactgatgtt tgtgcagtaa cttgggagtg tggtttcttt ttgaatcttt aattaaaacc 1620  
tgggattata tatccctgat aaatattcac acttgaacca tagttactgt aaaaagcaaa 1680  
aaatcttaat actgttatth tttgactttt ttcttaataa ttttttatat atatgcatat 1740  
atatatgtgt gtgtgtgtgt tgcttatgtt gttttgtaca gatgtgggac accattgcaa 1800  
caaaatacat tctttttgct ctaaaatatt tatgaagaaa atacttaaat gttatgtata 1860  
tgggtgtaat aagggaaaaa tcaagtatta taaacaagaa tgaaggtttt tgtaagatt 1920  
tctgttcagc gttttgcaag gtaaaatttt aggcaagttt tccctgaagt tatgtgtatg 1980  
tgagtattct cattcttccc aacttgcctt tgaagagtga aataaccatta ttatcaagta 2040  
gactactgtt cagcttttat tctgcccctg ctgtttatcc cttaagaatg agtttcttag 2100  
acttttccaa tatgtgattt tttttcccat ttgaatggt gattttaaat gtgtgagtgc 2160  
atgtactatc ttatctcaga tatttgcacc ccaatctgc ccccaactcc caaaagctag 2220  
aacactgcca actgatctgt tataggctct ttagaaacac ataattaaca cttagggtt 2280  
ggtgctgcta attctttgca aaaatccaaa tattgttaag ggaccaggga gatgccata 2340  
ccccttgatt ttccatctaa aaatatacat gtttatgtaa acaaatcttt ccatatccat 2400  
agtactttt caagtattta agcctaaaga ttttgatctc acatttttat acctgtttta 2460  
attgctcaca gttattacat acacatcagc catcaactaa agttgtactt taaaaattta 2520  
ctacaatatg tacatttcta agtcaaacac ttgtgacttt tgctttaatt ccatgaatgt 2580  
tcttgcctcc ttgatatttg tatttattct ttttttctct agagtagagg tataattgtg 2640  
tgatatttca gaaatacaga taaatgattc aaaaagtcac agttaaggag aatcatgttt 2700  
ctttgatcat gaataactga ttagtaagtc ttgcctatat tttcctgata gcatatgaca 2760  
aatgtttcta aggtaacaag atgagaacag ataaagattg tgtggtgttt tggatttgga 2820  
gagaaatatt ttaattttta aatgcagtta caaattataa tgtattcata tttgtacttt 2880  
ctgttaaaat gcatgattgc agaattgttt agattttgtg tttattcttg atgaaaagct 2940  
ttgtttgttc ttgtttttaa gtttgcactc aaatcttaag aaataaatcc acccatgtta 3000  
tcaaaaaaaa aaaaaaaanc ccgggggggg gcccggaacc aaatccnccc aaggggggnn 3059

<211> 1682  
 <212> DNA  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (52)  
 <223> n equals a,t,g, or c

<400> 101  
 ggcacgagga tggawgctg atgggggtgca gacacagatg gcaccccagg rntgtgccat 60  
 tccaccagac gtctcctaag acagagtttag agtcaacaat ctttggcagt ccgaggctgg 120  
 ctagtgggct cttcccagag tggcagagct gggggagaat ggagaacttg gcctcttatac 180  
 gatgaattaa gcaacaatgt aactgggtctt gacttgatcat attcccccat gcaatcctag 240  
 gtctgtattg ctcaatttta ggaagccttt gctactccat cagtaggttt agatttgagc 300  
 ttttgagacc tggctatgga aaagaaagac acttgagaat ttagtggttg ggtctgtaca 360  
 gatgatgcta cccaatttggt ctttgaagga tcaagtaaca ggttgaaaac tattttttata 420  
 aaggtaatac tttttcagtt cccttcttcc ttccctctca atccactagc tttcatgttg 480  
 ggcaaggaaa agttgaggaa ggatggctga tggatgatgga aagctgtgtt aatggatga 540  
 ggaatgtgtg aaaagtatac acaaagggct ctgaagctca agtcagagga gtgggaggtc 600  
 tgatcattgt tgggtgaaaa acgtaagggtt attttgtgtt tttaagttgg ttttacaatt 660  
 ctttctggg gaaattatct ctggagggga aaaagatcca ttctacgtat ccttgtggag 720  
 aaaagctaaa taacctttta gaatgtgggt ggtattggag aaagaagatg aattatagct 780  
 ccggaagaatc aagatcttaa gtgaagcctt tctgttcaga tgtgatctat aaaaaatcat 840  
 aatttgggga aagtttaagc aaatctggct ttgtagtctt gatgttataa gtgactttgt 900  
 gatcaaaactg tcaggcttgg gttcttgtta tagaatgctt ggtatagaaa aaccatgcca 960  
 tcattaatgg ctaacaacac gtagggactt catgtcatgt caaagatagc tctttgcaag 1020  
 tgccttgatt aaaccagaaa actgtcatcg ttttaaccaa atatctgaat ggatcatctg 1080  
 taactcatgg gtttttggcc tcataagatg gtccactctg tacacaggca ttcctcctgc 1140  
 aataatgttg tatctttgag accgttgtca gtgtacacaa ctcacatcct tcatattgaa 1200  
 ggtgactcat ttttctgcac acttttttga tgtgatgctt gacgtgaggc ccgacactag 1260  
 gattctcaat gcaagaatcc agtaccttgc acatagaagt agcaacccat cccttgccata 1320  
 ttttcatctt gctgttttct tttttttaa aaaatggatg tgacttgttt tgaatgtttt 1380  
 gtattatact tgtttttgtg tgtgcataaa ttcattctgt aggatcttaa gaaaaagagt 1440  
 ccagaatgt tgcttctatt attgtgcaca accattgaga ggtgttacia gaatgcagtt 1500  
 aattttaaca tgtgtgatgt gccatgggtg aaaagtacta tcggaataac tctgcagtga 1560  
 cagaatttga agtttggtc gcatccatac ttttctactg taaatatttc actctcctct 1620  
 agctatcctt gatgagcttc tcactttaag aataaatgtg tttgatataa aaaaaaaaaa 1680  
 aa 1682

<210> 102  
 <211> 938  
 <212> DNA  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (30)  
 <223> n equals a,t,g, or c  
  
 <220>

<221> misc feature  
<222> (812)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (913)  
<223> n equals a,t,g, or c

<400> 102  
cccacgcgtc cgtccgggtg ctgcgcgcgn gacctggacg cagagaagcc agagactttc 60  
gcttcgggct gccgcaggct tcgctgggtc aggttaagctc cgcacactct cggccgggtcc 120  
cgagtccgac tccctcaagg gtgacgcgag ctctgccctt taaccggaaa cgtctccctg 180  
ctcaccacac cccgcgcgag acgcagtgtc gagcacacag ctaccggaca aagagtgcg 240  
cccggagctg gagttatggc ggctacggag ccgatcttgg cggccactgg gagtcccgcg 300  
gcggtgccac cggagaaact ggaaggagcc ggctcgagct cagcccctga gcgtaactgt 360  
gtgggtcctt cgtgtccaga ggcctcaccg cctgcccctg agccttccag tcccaacgcc 420  
gcggtccctg aagccatccc tacgccccga gctgcggcct ccgcgccctt ggagctgcct 480  
ctcgggcccc caccggtgag cgtagscctc aggccgaagc tgaagcgcgc tccacaccag 540  
gtcccgcccg ctctagactc ggtcccga ga cgttccgcca gcgtttccg cagttccgct 600  
accaggtatgc ggcgggtccc cgggaggctt tccggcagct kcgggagctg tcccgccagt 660  
ggctgcggcc tgacatccgc accaaggagc agatcgtgga gatgctggtg caagagcagc 720  
tgctcgccat cctkcccgag gcggctcggg cccggcggat ccgccgccgc acggatgtgc 780  
gcatcactgg ctgagcgggt gagctgcggg cngccagggc cgggcgctct gtgcggactg 840  
gggccatgat cgggcccggg ggcctgagcc tgggacccca ccccggtgta atgaaaaatg 900  
agttttggca gcnaaaaaaa aaaaaaaaaa aagggcgg 938

<210> 103  
<211> 2012  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1993)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2002)  
<223> n equals a,t,g, or c

<400> 103  
gctggataat tccagcctgt tagctactca caggaacatg cagaattatt ggctccaggg 60  
agttttggag aaagaagggt tacgttttca aacttacaga taacagttga catcaatgct 120  
tctctttccc agaacaatct ggagtgtgcc agaaaactct gtaaacagga gtcgtgctgt 180  
gtgtgaactg taaactcttc tctccaggcg tcgaggggac ctttgcttta ctttgcagct 240  
gggtacatc agacgtgtgc attggaacaa taaacttcct taactgggaa aagaatgctt 300  
ctctgtcttc maaatarttc tgctatgtga catttttgc atcatgaatt ttacatcagt 360  
gmtagctctt tgttttacgt gtttcattkg gcaggtcaca aaggctcttg gctaccacac 420  
atacgtgcat acacacacac acacacacac acacactcat aaaggatttt 480

```
cttttctgct ttaccttta ttttcagtct acttggttg taatgaaagg tagagcctta 540
tttttgaact atatcccaac agaatcgaat ttccattttg ccaagaatta taaaaccctg 600
aggttttaaa attcagtttc ttttctgggg atttaacatg gaaggacttg gagggcaaat 660
ggsccagtga ttggaaaargg gaaaaacaaw tcatttcatt taaaattatt caataacat 720
tgccagcatt tgggattctg agtgctgttt atgaagccct ttcattgata taatttcac 780
tatctctcac aaggctgtaa gcaattccta tgtccatatg gcagtgaagg aatggagatt 840
tgagcagggt aaggaggtt tcacctggaa gctcttcttt tttttccttc tgccacagta 900
rggtcatcag actgtcagcc ccagcactgg gagccgagta acacgcatgt tctcattaat 960
atccttttct catgttttta ttaaagatat atgcaagttg ccgaaagacg aaggaaacttg 1020
cagggatttc atattaaaat ggtactatga tccaaacacc aaaagctgtg caagattctg 1080
gtatggaggt tgtggtggaa acgaaaacaa atttgatca cagaaagaat gtgaaaagg 1140
ttgcgtcct gtgctcgcca aaccggagt catcagtgtg atgggaacct aagcgtgggt 1200
ggccaacatc atatacctct tgaagaagaa ggagtcagcc atcgccaact tgtctctgta 1260
gaagctccgg gtgtagattc ccttgcactg tatcatttca tgctttgatt tacactcgaa 1320
ctcgggaggg aacatcctgc tgcattgacct atcagtatgg tgctaattgt tctgtggacc 1380
ctcgtctct gtctccaggc agttctctcg aatactttga atgttggtgta acagttagcc 1440
actgctggtg tttatgtgaa cattcctatc aatccaaatt ccctctggag tttcatgtta 1500
tgctgttgc aggc aaatgt aaagtctaga aaataatgca aatgtcacgg ctactctata 1560
tacttttctg tggttcattt tttttccctt ttagttaagc atgactttag atgggaagcc 1620
tgtgtatcgt ggagaaacaa gagaccaact ttttcattcc ctgcccccaa tttcccagac 1680
tagatttcaa gctaattttc tttttctgaa gcctctaaca aatgatctag ttcagaagga 1740
agcaaaatcc cttaatctat gtgcaccgtt gggaccaatg ccttaattaa agaatttaaa 1800
aaagttgtaa tagagaatat ttttggcatt cctctaattg tgtgtgtttt tttttttgt 1860
gtgctggagg gaggggattt aattttaatt ttaaaatgtt taggaaattt atacaaagaa 1920
actttttaat aaagtatatt gaaagttaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 2012
```

<210> 104

<211> 1094

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (26)

<223> n equals a,t,g, or c

<400> 104

```
tcctcctggg aagcctggcc tgccncccc gcaaaagggtg tttttgcgct ggttcaatga 60
atagatgatg cagaggcccc attggagaca cgtgaatggc gtgtgcgcc atcagttccc 120
ggctgggggg cagggtgtgc ttgggcccc gccctcggc cggcgtgtgc gagtgcgccc 180
ctggctgtga gtgtgaccg ttcctctccc ctgtacatag cmcgagccag tcctgagtgg 240
gtgactcctg agtgggtgac gcgcagacgg gatttctcag gtcatttgta tggctgacat 300
gatggctgct gctttggctg ccaccacccc cgggcccage ctgtctgaaa ttcagggttt 360
aggccgaaaa acccggtggg gaggggtggg gagccggagm tctgtggcgg ggctggagg 420
ctggggtgca cttagtttg gggcgggacg ggagccggc ttgtgactgg cgtggtctgg 480
ctgctgctcc cgaacggagg ggtcggggtt ggcttgcctg gccctcagag ccagtggtg 540
ggctctgact cggctcccta ctccctgcac ccagctgggc gcaactgggg cctgcggtcg 600
gaatgtatcc ctccctcag ttttaacctg agctgccgaa cgcacagtgg gccggggcg 660
aggctggggg aagcggggcc caattacgga tcccgggagt tacagggtgc gacgtgatgt 720
cgctctctg gtgcccagct ccctcctgg tctgagacta gctctggggg tggcggggg 780
```

```

ccccamacgc tgctcccgct ccaccctgcc cgtgctgctg ctctgtgcct gctgtcagag 840
ccctgggtggg ggaggatgtg gccaccctga gaccgggagg agacgggagc ctgcctgggt 900
ttgcggagag cgcgttatgg gtgtggtccg tccagacacc ttgtttcaag ggggatgggc 960
gtgagcgggc aagcagagca tccccaccgc tgagcaagaa ctttttcttg tttttaaac 1020
atcacgtcct catttcacat tggaataaag tgagtttttg aaacctgcga aaaaaaaaaa 1080
aaaaaaaaaa attc 1094

```

<210> 105

<211> 2297

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (30)

<223> n equals a,t,g, or c

<400> 105

```

agctcgtgcg cccgccgtgc cgggtccggan attcccgggt cgacccacgc gtccgatctg 60
tctgcacca tctgcctaata tcttccctca cagtctgtag ccatctgata tcctagggga 120
aaaggaaggc caggggttca catagggccc cagcgagttt ccaggaggtt agagggatgc 180
gaggctaaca agttccaaaa acatctgccc cgatgctcta gtgtttggar gtgggcagga 240
tgagaacag tgctgtttg ggggaaaaca ggaaatcttg ttaggcttga gtgaggtgtt 300
tgcttccttc ttgccagcg ctgggttctc tccaccagc aggttttctg ttgtggtccc 360
gtgggagagg ccagactgga ttattcctcc ttgtctgatc ctgggtcaca cttcaccagc 420
cagggctttt gacggagaca gcaaataggc ctctgcaaat caatcaaagg ctgcaaccct 480
atggcctctt ggagacagat gatgactggc aaggactaga gagcaggagt gcctggccag 540
gtcggctctg actctcctga ctctccatcg ctctgtccaa ggagaaccog gagaggctct 600
gggctgattc agagggtact gctttatatt cgtccaaact gtgttagtct aggccttagga 660
cagcttcaga atctgacacc ttgccttgct cttgccacca ggacacctat gtcaacaggc 720
caaacagcca tgcatttata aaggctcatca tcttctgcca cttttactgg gttctaaatg 780
ctctctgata attcagagag cattgggtct gggaagaggt aagaggaaca ctagaagctc 840
agcatgactt aaacaggttg tagcaaagac agtttatcat caactctttc agtggtaaac 900
tgtggtttcc ccaagctgca caggaggcca gaaaccacaa gtatgatgac taggaagcct 960
actgtcatga sagtggggag acaggcagca aagcttatga aggaggtaca gaattattct 1020
tgcgttgtaa gacagaatac gggtttaatc tagtctaggc accagatttt tttcccgctt 1080
gataaggaaa gctagcagaa agtttattta aaccacttct tgagctttat cttttttgac 1140
aatatactgg agaaactttg aagaacaagt tcaaactgat acatatacac atattttttt 1200
gataatgtaa atacagtgc catgttaacc taccctgcac tgctttaagt gaacatactt 1260
tgaaaaagca ttatgttagc tgagtgatgg ccaagttttt tctctggaca gkaatgtaaa 1320
tgtcttactg gaaatgacaa gtttttgctt gatttttttt tttaaacaaa aaatgaaata 1380
taacaagaca aacttatgat aaagtatttg tctttagat cagggttttg ktttgkttt 1440
ttaattttaa aatgaacccc tgccccctcc ccagcaaagt cacagctcca tttcagtaaa 1500
ggttgagtc aatatgctct ggttggcagg caaccctgta gtcattggaga aaggtatttc 1560
aagatctagt ccaatctttt tctagagaaa aagataatct gaagctcaca aagatgaagt 1620
gacttcctca aaatcacatg gttcaggaca gaaacaagat taaaacctgg atccacagac 1680
tgtgcgcctc agaaggaata atcggtaaat taagaattgc tactcgaagg tgccagaatg 1740
acacaaagga cagaattcct tcccagttg ttaccctagc aaggctaggg agggcatgaa 1800
cacaaacata agaactggtc ttctacactt tctctgaatc atttaggttt aagatgtaag 1860
tgaacaattc tttctttctg ccaagaaaca aagttttgga tgagctttta tatatggaac 1920
ttactccaac aggactgagg gaccaaggaa acatgatggg ggaggcagag agggcaagag 1980

```

```

taaaactgta gcatagcttt tgtcacggtc actagctgat ccctcaggtc tgctgcaaac 2040
acagcatgga ggacacagat gactctttgg tgttggtctt tttgtctgca gtgaatgttc 2100
aacagtttgc ccaggaactg ggggatcata tatgtcttag tggacagggg tctgaagtac 2160
actggaatth actgagaaac ttgtttgtaa aaactatagt taataattat tgcattttct 2220
tacaaaaata tattttggaa aattgtatac tgtcaattaa agtggttttg tgtaaaaaaa 2280
aaaaaaaaaa actcgta 2297

```

<210> 106

<211> 442

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (419)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (423)

<223> n equals a,t,g, or c

<400> 106

```

tcgacccacg cgtccgcctg tgggacgcgg tgggtggccgt tgggtcggga gagtgagcgg 60
tatttgcmtc gtttttcttg cttgttttcc ccccgttaga ctttgtcggg agagcgcggg 120
tatgggcccgc aagaagaaga agcagctgaa gccgtggtgc tggatttgta atagagattt 180
tgatgatgag aagattctta tacaacacca aaaagcaaaa cattttaaat gtcataatg 240
tcataagaag ttgtacacag gacctggctt agctattcat tgcattgcagg tgcataaaga 300
gacaatagat gctgtaccaa atgcatacct gggagaacag acatkgattg gaaatatatg 360
gtatgggaarg tattccagaa aaagatatkg atgaaagaag acgacttctt ggaacagana 420
acnccagaga gtccaaaaaa ag 442

```

<210> 107

<211> 1019

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (995)

<223> n equals a,t,g, or c

<400> 107

```

ttgatctgcg gctgtcgagg cctgaggcag tggaggctga ggctatgatg gcggccatgg 60
cgacggctcg agtgccgatg gggccgcggg gcgcccaggc gctctggcgc atgccgtggc 120
tgccggtggt tttgtcggtg gcggcgccgg cggcgccggc agcggcggag cagcaggtcc 180
cgctgggtgct gtggtcgagt gaccgggact tgtgggctcc tgcggccgac actcatgaag 240
gccacatcac cagcgacttg cagctctcta cctacttaga tcccggccctg gagctgggtc 300
ccaggaatgt gctgctgttc ctgcaggaca agctgagcat tgaggatttc acagcatatg 360
gcggtgtgtt tggaacaag caggacagcg ccttttctaa cctagagaat gccctggacc 420
tggtcccttc ctactggtg cttcctgccg tcgactggta tgcagtcagc actctgacca 480

```



```

cttacctgca ggagaagctc ggggccagcc ccttgcatgt ggacctggcc accctgcggg 540
agctgaagct caatgccagc ctccctgctc tgctgctcat tcgcctgccc tacacagcca 600
gctctgggtct gatggcagcc agggaagtcc tcacaggcaa cgatgaggtc atcgggcagg 660
tcctgagcac actcaagtcc gaagatgtcc catacacagc ggccctcaca gcgggtccgcc 720
cttccagggt ggcccgatg tagccgtgg tggccggagg gctaggctcg cagctgttac 780
aaaaacagcc agtatcacct gtgatccatc ctctgtgag ttacaatgac accgctcccc 840
ggatcctgtt ctgggcccac aacttctctg tggcgtacaa ggaccagtgg gaggacctga 900
ctccctcac ctttggggtg caggaaactc acctgactgg ctcttcttg aatgactcct 960
ttgccagcty tcactgacct atgaacgact ctttngtacc acagtgcacat taaagttat 1019

```

<210> 108

<211> 711

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (642)

<223> n equals a,t,g, or c

<400> 108

```

cttgaaaact tagtttacta tacatcttgc cctattaata tgttctctta acgtgtgcc 60
ttgttctctt tgaccatttt cctataatga tgttgatgtt caacacctgg actgaatgtc 120
tgttctcaga tcccttggat gttacagatg aggcagtctg actgtccttt ctacttgaaa 180
gattagaata tgtatccaaa tggcattcac gtgtcactta gcaaggtttg ctgatgcttc 240
aaagagctta gtttgyggtt tcctggacgt ggaacaagt atctgagttc cctggagatc 300
aacgggatga ggtgttacag ctgcctccct cttcatgcaa tctggtgagc agtggtgagc 360
gcggggagcc agagaaaact gccagttata taacttctct ttggcttttc ttcactctga 420
aaacaaggat aatactgaac tgtaagggtt agtggagagt ttttaattaa aagaatgtgt 480
gaaaagtaca tgacacagta gttgcttgat aatagttact agtagtagta ttcttactaa 540
gaccaataac aaatggatta tttaaaccaa gtttatgagt tggttttttt cattttcyat 600
ttgtatttta ttaagagtgc ttttcttatg gtgatttttt tnaattgcga ttgatattgg 660
tttgccata tggccccacc caaatcccca tcttgagta taatccccat g 711

```

<210> 109

<211> 743

<212> DNA

<213> Homo sapiens

<400> 109

```

tcgagttttt tttttttttt ttttactttt taaaatttta ttgatgtacc acctgatcaa 60
agcatgggat attttaatag tattatacat aatattttta catagaaaac tttacatagc 120
atttcatatt atataattct gcttattctt tcaaaaattt atacatccat tgggcaagga 180
atggttttca ttaaattacc aatattaaat gcacttaatc attgtgtata ggttaaacca 240
aagtaactat taactaactt ttaggcattt taaggaggta aaacatacat tttacacata 300
aatatttgat gcaaatatgc agataaaatt ttttaaaaat tagaactctg agtaaaacac 360
ctttgataga ttatattggt ttgttttgag agcaaggatt tccagatatg ttcattcttt 420
aaaacactca gctttggtt ctttgtttcc caaactgcaa agctgctgat aacaaaactc 480
caggattcca tgtgagtcca gctatgtcta ctttaacaca aatattaaaa cagaattcag 540
raaatgcagt attaaggatc cagcttctat tgaaaccaat atccatttgc atcataacaa 600
caaacatttg aatgagatgg tcacacttgt acttatcagc aggttccttt aataacaaag 660

```

actactaaat gtatatacctt aatcacaaaa gaacaacaaa aaaaatacag gttttttttt 720  
tttcatttcg tacaaaagtc acc 743

<210> 110  
<211> 795  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (2)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (645)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (737)  
<223> n equals a,t,g, or c

<400> 110  
tnctaaatat cagatgtctt tgatgtaagg gtagggaatg gagaaatatt ttcaattgtg 60  
tatttgtatt acaaagaact tgaaatttac tttcttagtt gattatatta aatgatgtat 120  
atattatatg tggtttataa gctcaacact ggccattttt ttagttttat tgttaaatgg 180  
tattttttcta tgtttaatta taatagatct ggctttttct ggatagcata aagatcactg 240  
aactatatat atataagara caagagttct atttttagcac aaaggcattt tatattattt 300  
attgaatoca taagtgtgtt ttcgtcaaaa acattccata ttatttctgc tcctttttat 360  
ttgtatagtt tgttatttaa agaaatggca gtccttcctg ttcttaatac aataaaattg 420  
aaataatgca cctagtaatg tggccgacat ctcttctcac caccatggac tgttttcaac 480  
aacagttgat cttctggtct gtgctgagag gcgcatgcat gtctttcgtc acgtcgggca 540  
gcacacctgc tgtgaaatac tgctttcatc tacctcttca gaaggcttct tgcttggtga 600  
caagtaccgc aaaggcttta ttctggactg gctatctcat aaaanggatt tctgtaagac 660  
tttgagtggt cattccctca gaaccyaggt ttgtttctaa agccacggta ttgtccrrgr 720  
rccctgtgtg ktggggncag gtagctatcc ctcccatgtc attagtaatc ctttaggatt 780  
ttaagggtaca atggg 795

<210> 111  
<211> 1332  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (6)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1194)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1237)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1241)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1300)  
<223> n equals a,t,g, or c

<400> 111  
ncgggncagc agctcccagt gtgacctgac aaaaacacgt aggggcaggg acggtcccca 60  
ccccagggga cacaaccctt ggtcttgac cagtagagga cacggagggt tcagaccct 120  
cctcagacc tccccacatc tgaaactgcc tcccccaac caccagcagc agcagggccc 180  
tcctcccca ccagctctcc ccacagggcc cctcagcatc atggagaccc gcagcggggc 240  
ttagccacc ctcaaaccga gggccccctg gcacctgggc tctggccgtg ttttctggcc 300  
agagcccccac tttcctaact cgtgctccct tccgccttct tttccgtact gtgaagaaag 360  
aactctccac ccagctccc accctgccct ggctgggtg gaggaactgt gcctccatcc 420  
ccagaagaaa cagccccctc tgctgctggg gtgggactgt ctgtgtgccc tgtgggggtc 480  
cgtgtgagca ggcccacctg gctccagacc cggcccaac ctgagacaga accaggctga 540  
gccaggcctc cacccccacc ccggtttgct gggggctcct ccagccgcc ccatggraag 600  
aggcctggta ccgctcacc cacagaggtc tgtgccagggt gcgcttctgc aggtggagcc 660  
aagctctccc tgaggccaga ggcggggcct gggccgggag ccaggggaa ggccaggctg 720  
gaccccggtc ycacaccac atccagcctg caggcctctc tgcatcctc tcacctccc 780  
tmagctcccc ttcctctgca gtcacctca gctcccttc cttgcccgc tctcccccg 840  
ccgccccacc agttaaaccg atgaccaaag acctttctta tgccggaagc aaaaaccaa 900  
actttttgtt ggctttttcc tttgtsgcct cccagcacc tgccctcca gtctcccacc 960  
ccggccccag gctggaagcc tccctccact taagttattg ttttaaacca aagtttacag 1020  
tgtctgttg tgccaagac cttctctctc caccctcct ccatccacc tgaggaccct 1080  
ggggctcagt ggaggcaggg ccctgcccc cttcccttc cggctcctgg ccagcctgg 1140  
ggggaaggga raaaggaggg gggaraaagc ggggttcttc acccctcag ggantggggc 1200  
acggggagcc ctttcttccc tggaccctgg ggcttgnttc ntgggggggc tcttccaaga 1260  
acccctcttc taagggaacc aagtttcacc cgttcgtggn tgggggatgt tgggatttct 1320  
aaggcaaaag ag 1332

<210> 112  
<211> 743  
<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (53)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (272)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (275)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (278)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (590)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (618)

<223> n equals a,t,g, or c

<400> 112

```

ttgctggtct gatccatgca catggccagg ctgctaggct cttgtgctgg gcnggaagtc 60
gggtgcggatg gccagctcca ggatgaccg cgggaccg ctcacaaata aggtggccct 120
ggtaacggcc tccaccgacg ggatcggctt cgcacgccc ggcgtttggc ccaggacagg 180
gccacgtggt cgtcagcagc cggaagcagc agaatgtgga ccaggcgggtg gcacgctgca 240
rggggagggg ctgagcgtga cgggcacctg tncantgntg gggaaaggcgg aggaccggga 300
gcggctggtg gccacggctg tgaagcttca tggaggtatc gatatcctag tctccaatgc 360
tgctgtcaac ctttctttg gaagcataat ggatgtcact gaggagggtg gggacaagct 420
ctggatggac aaggaaaaag aggaaagcat gaaagaaacc ctgcggataa gaagggttagg 480
cgagccagag gattgtgctg gcatcgtgtc tttcctgtgc tctgaagatg ccagctacat 540
cactggggaa acagtgggtg tgggtggagg aaccccgccc cgcctctgan ggaccgggag 600
acagcccaca ggccagantt gggctctagc tcctggtgst gttcctgcat tcamccaytg 660
gscttttccc acctygytc amcttactgt tcacctcatc aaatcagttc tgccctgtga 720
aaagatccag cttccctgc cgt 743

```

<210> 113

<211> 1690

<212> DNA

<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1659)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1664)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1676)  
<223> n equals a,t,g, or c

<400> 113  
aattcggcac cactcagtcc cacaggcctc ggccaggagc acaccggcca cgtccgcttc 60  
ttggctgcag tccagctgcc agatggcttc aacctgctct gcccaacccc accacctccc 120  
ccagacacag gccccgagaa gctgccatca ctggagcacc gggactcccc ttggcaccga 180  
ggccccgccc ctgccaggcc taaaatgctg gttatcagtg gaggtgatgg ctatgaggac 240  
ttccgactca gcagtggggg cgccasagca gtgagactgt gggtcgagac gacagcacia 300  
accacctyct cctgtggagg gtgtgacctt gtctgccctg gcccaggact sgcccgccca 360  
cctgccttca gcctgcttgc ctctccctag cccacacgca gactttgacc aggagtatcc 420  
agccaggggg cacatgtgcy kgcrtgggct ctgcttgtct tcgcggaaga ttcctgatgg 480  
aacacccact ggccagccag gccatggctt ctcccgaccc tctggctgcc ccggtgcttc 540  
cagtcgatgat cgggtggggg acatgtgggc tgaccaggac ctctgacctt ggagcttcta 600  
ccaaagacac agctgggtct ggacccacag ggsstgggga gggccatgtg caatatttgg 660  
agggttttct ggagggcagc aggaaggctg gggaattccc catgtacagt atttatgttt 720  
cttttttagat gtgtaccttc ccaagcactt atttatgcag tgacctggtc acctgggggtg 780  
ggggtgattt gaggaatga catgaggaaa agaaacctat tcctgccctg gggaccaccc 840  
tgggactcta accaagcctt cctggaggga cccatgcgcc cctgagcccc attccattca 900  
tacagacaca cactgtacga cactgcatgt ccaaggccct aaacattgcc cgttgacata 960  
aactttccag ggccccagcc tgatggggct gccctcagtc ctctagatca agatgctgac 1020  
tattaggggg cagtgtattgc catctgggga cctgtcaggc tttgtcattt cccagtttgt 1080  
tggtgggtgcc tttagtgggt ccctaatttg ggaacactga tggggccttg gacagggctt 1140  
tctctcaggt aggagaaatg ggcccatgat ctctcacag tcgccccag tccttgcccc 1200  
tgcttcctg tgtctcatgc actggcacat atggtcacct tggagggcag acctaggagc 1260  
ccctctgacc actgaatccg tctccacacc ccttctgcca agggaaagccc cttcagggaag 1320  
gaccccccaa agctgagggg ctgaatgtag ctttttcaac agagaaggct cccacttgag 1380  
agcagcctct acctgacccc ctggaccaca gagagccact ctgaccctca gccccctcgc 1440  
ttcttcagct aaaactccaa aggtttgggt tcagatgggg tttgttttgt tctgttttgt 1500  
tttggttttg tttggggtgg gtgggtcatt gcggtcttag attatgtttc tcttgctacc 1560  
aaacagtcac gtattaactc tctttggatg atgaagttaa aagagtcaat aaatagaaac 1620  
accagatgac tgcaaaaaaa aaaaaaaaaa aaaaaaana aaanaaaaaa aaaaaanaaa 1680  
aaaaaaaaaa 1690

<210> 114  
<211> 620  
<212> DNA  
<213> Homo sapiens

<400> 114  
ctctgggcct gggctctgggg gagaggggtg ccagggagac tcagctctcc ttgggggctg 60  
gccagctgac tgaggggtaca caggattggg tctagacctt gatgcctggg tggagggccc 120  
ttgtaagggg ccatagcctc ttcaggacca actggaggga gagttaggaa acaccagctc 180  
ctgcctgggg cagtgaggga atgggagcag ctgtgggcgc ctcatctcag gcaagtcctc 240  
cccaaacctt cagatgcagt gagacctggc ctccctgttg tgcttttcag actttgtttt 300  
cagaatgctt ttatctcgag tgtgcccttc ggccctcaca agagcccctg gggagtaggt 360  
ggtggcctgt gccgtcatcc ccatttcaaa gcagggagct gaggtcctg gaggggaaaag 420  
tgcttgccctg aggtcccact gtgttagtgg gtgggcagga ctggaactcg gttctccaac 480  
agcccagagc tcaactctttt acaccagag gtggagcagg tggcttaggg ggtgggttatg 540  
tacttcacaa gccaatcccc ttcagccagg agctcctggg tgcatttccg tgtcagaaac 600  
agtaccgagt cccacccct 620

<210> 115  
<211> 542  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (392)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (412)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (511)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (521)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (535)  
<223> n equals a,t,g, or c

<400> 115  
tcgacccaag cgtccgcttc tcggccctt gtagaacctc tgtcaggttc agcctactcg 60  
cctctactcc agcctccact ccggcctcca ccatgtccgt caggtgacct agaagtccta 120  
caaggtgtcc acctccggcc cccgggcctt cagcagccgc tcctacacca gcgggcctgg 180  
ctcccgcacg agctcgtccg ccttctcccg ggtgggcggc asttccgggg gggcctgaac 240  
agcagcatga gtgtggtcgg gggctacggc ggcggggccc gggatatggg ggcacacgg 300  
ccgtctcagt gaaccagagc ctgctgagcc cccttwaagc tggaatkga tcccaacatc 360

```

caagctgtgc gcaacccagg agaaggagca gntcaagacc ttcaacaaca anttggttc 420
gttcacgcac aagtgaagca ctggagcagc agaacaaatt tttggagacc aattggagct 480
tcttaaagca gcagaagacg cgcggagaac ntagacaaat nttcgagagt aaatnagaac 540
tt
542

```

```

<210> 116
<211> 525
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (420)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (424)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (517)
<223> n equals a,t,g, or c

```

```

<400> 116
aattcaaccg tcgttatccc aaaattcagt ttccactttc caccggccct tccggcacta 60
tgctggatgg tgtactggag ggaaaactga atgcggcggt tattgatgga cccattaacc 120
atactgccat cgacgggata ccggtatacc gcgaggaact gatgatcgtc acgccacaag 180
gatatgcgcc agtaacccgt gccagtcagg ttaatggcag taacatttat gccttccgcg 240
ccaattgttc gtatcgtcgc cacttcgaga gctggtttca tgctgacggg gccgctcccg 300
gaactatcca tgagatggag tcttatcacg gaatgttggc ctgtgtgatc gcaggagcag 360
gcattgcgct tattccgcgc tctatgctgg aaagtatgcc ggggcatcac cargttgaan 420
cgknggccgt tagctgagca atggcggttg ttaacaacct ggctggtctg gccgtcgttg 480
tgcgaaaaaa cgttccgctc gaaggggggc ccggtancca attcg
525

```

```

<210> 117
<211> 728
<212> DNA
<213> Homo sapiens

```

```

<400> 117
aacgagcgcc tgctaggatc agcgggtggtg gttccgcgat ggtaggcggc ggcgggggtcg 60
gcggcgccct cctggagaat gccaaacccc tcatctacca gcgctctggg gagcggcctg 120
tgacggcagg cgaggaggac gagcaggttc ccgacagcat cgacgcacgc gagatcttcg 180
atctgattcg ctccatcaat gacccggagc atccactgac gctagaggag ttgaacgtag 240
tagagcaggg gcgggttcag gttagcgacc ccgagagtac agtggctgtg gctttcacac 300
caaccattcc gactgcagc atggccaccc ttattggtct gtccatcaag gtcaagcttc 360
tgcgctccct tcctcagcgt ttcaagatgg acgtgcacat tactccgggg acccatgcct 420
cagagcatgc agtgaacaag caacttgcat ataaggagcg ggtggcagct gccctggaga 480
acacccacct cttggagggt gtgaatcagt gcctgtcagc ccgctcctga gcctggcctt 540

```

tgacccctca gcctgcatac tggatccctg gtcccagctc ctgccagggc tgttaccgtt 600  
gttttcttga atcactcaca atgagaaact aacattttgc tttttgtaat aaagttaatt 660  
tatattcarw tcaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa acccgggggg 720  
gggcccc 728

<210> 118  
<211> 948  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (920)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (944)  
<223> n equals a,t,g, or c

<400> 118  
agaagtacgg acccctgaag cccctgccac agaccccgca cctggaggas gacttgaagg 60  
aggtgctgcy ttctgaggct ggcatcgaac tcatcatcga ggacgacatc aggcccgaga 120  
agcagaagag gaagcctggg ctgcggcgga gcccatcaag aaagtccgga agtctctggc 180  
tcttgacatt gtggatgagg atgtgaagct gatgatgtcc aactgcccc agtctctatc 240  
cttgccgaca actgccccct caaactcttc cagcctcacc ctgtcaggta tcaaagaaga 300  
caacagcttg ctcaaccagg gcttcttgca ggccaagccc gagaaggcag cagtggcccc 360  
gaagccccga agccacttca cgacacctgc ccctatgtcc agtgcctgga agacgggtggc 420  
ctgcgggggg accagggacc agcttttcat gcaggagaaa gcccggcagc tcctggggccg 480  
cctgaagccc agccacacat ctcgaccct catcttgtcc tgaggtgttg aggggtgtac 540  
gagcccatc tcatgtttac aggggtgttg ggggcagagg ggtctgtga atctgagagt 600  
cattcaggtg acctcctgca gggagccttc tgccaccagc ccctccccag actctcaggt 660  
ggagcaacag ggccatgtgc tgccctgttg ccgagcccag ctgtggggcg ctcctggtgc 720  
taacaacaaa gttccacttc caggctctgc tggttccctc cccaaggcca caggagctc 780  
cgtcagcttc tccaagccc acgtcaggcc tggcctcatc tcagaccctg cttaggatgg 840  
gggatgtggc cagggtgtct cctgtgtcga ccctctcttg gtgcattttt ttggaagaat 900  
aaaattgcct ctctctttgn aaaaaaaaaa aaaaaaaaaa gggnggcc 948

<210> 119  
<211> 211  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (123)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (125)



<223> n equals a,t,g, or c

<400> 119

```
tcgacccacg cgggtccgctt ggtgggggtcg gctgctttct cgcgtttccc cccaaccccg 60
tccggcctcg cccagcgttt ccacgcggaa ccaactgcca gaggcgcggc gcggcgtcga 120
gcngngcgag tgtgaggaaa ccgccgcctc agccgagcgc gcgggcccgc ccagggcggt 180
agttttcggc gcgcagtcgc ggtcccccg c 211
```

<210> 120

<211> 1308

<212> DNA

<213> Homo sapiens

<400> 120

```
tcgacccacg cgtccggact gttctaagt agttcgggtg ggggagcttc acgaggggag 60
gctgctctgt gaaggaaccg cctttctctc cgcggtgtct acccttttct ccccatatct 120
gtttggacat gagctgaggg cacggtcgcg ggcggtcagc ctgttcgcag ctacggcgag 180
gaggggcgcg attgytcctt gttgccgctc cgcttagtgg ccgcgtccat tccgcgcggt 240
gtcccgatth tagggtagg gagaagtgtc agcttcaggc atcgcgaggc gtggcgggcc 300
catggccccc tggggaggg ccccgcggt ggtactgctg ttcagcggca agaggaaatc 360
cgggaaggac ttcgtgaccg aggcgctgca gagcagactt ggagctgatg tctgtgctgt 420
cctccggctc tctggtccac tcaaggaaca gtatgctcag gagcatggct tgaacttcca 480
gagactcctg gacaccagca cctacaagga ggcttttcgg aaggacatga tccgctgggg 540
agaggagaaa cgccaggctg acccaggctt cttttgcagg aagattgtgg agggcatctc 600
ccagcccatc tggctggtga gtgacacacg gagagtgtct gacatccagt ggtttcggga 660
ggcctatggg gccgtgacgc agacgggtccg cgttgtagcg ttggagcaga gccgacagca 720
gcggggctgg gtgttcacgc cagggggtgga cgatgctgag tcagaatgtg gcctggacaa 780
cttcggggac tttgactggg tcatcgagaa ccatggagtt gaacagcgcc tggaggagca 840
gttgagaaac ctgatagaat ttatccgctc cagactttag ttagtaggtt ctaggagtga 900
gctggggcct gctgaggtgg ggggtgggct gactctgcaa aatgggggtg tccccgatc 960
ctggccgagg tgaggaacag acaggggggg tctagattct gagggggttg gtggatattg 1020
ggcaaggcag gaaacctctg gagacctcat tttctccatg gggaagacag ccatgctctt 1080
caggaggaga ctccaagggc aaaggagggt gtcttggtg tgcttgaagg cgaaacctg 1140
ccatatcccc agtgccagtc ccctcagcct gtggtggcct tgcacctga ctggatgttc 1200
tcagcccctt gttctgggca agaaccaga gtcgccaggt gtggatacta ataaacctct 1260
tggagcacia aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaagg 1308
```

<210> 121

<211> 2516

<212> DNA

<213> Homo sapiens

<400> 121

```
gattgacatt ccagtgaat gatgggagtt aattgattta atttagatta gttgaaaatt 60
attacaaaat attctaaaag ggttttttgt ggtacttcaa gaaacctgat tagttttgat 120
ctattgaaat cacaaaagta gaacagggcw ytttattttt gtataattta ggattaggta 180
tgcttctttt ttctaacaag tcatgttttc taacccttct ttcactaagc aaaccagaac 240
agatttgaaac tgttatgggt tatatatttag tatggagatc agctcagatg acattaaaaa 300
tgccgtagtg ttattcttgt atgccaaatc tttttttccc caaaatttag actttaattt 360
tatttactgt tataatattt gttttcttag attaggtagg aaatcttaat ttggccaccg 420
cctactttga caagtaaata ttacatcata cgattttgca acattaaatt agaacactag 480
```

```

aaactaaaaa attatgtttc agtgaatgct acaactaagc attttttttt ttttaagaaa 540
acaattgtat tatgttttgt tgccttgcca ctttgagtat cttatctgaa aatctgttcc 600
ttgccatggt tttctcctgt taacataaac tatgtgccct gtgaatttct ggggactgaa 660
tttgaaattg ctccctgcaa ccgtttgtgg cctggcgtgt atctgaatgc ctgaatatct 720
ccccgctgaa tgaatttcgt attctgccct gaattcactc gggatatattg attggctgga 780
tgatcttggt gccgccact tgacgtttcc agaagagtca ccgaagaaa gaaccaggag 840
tgtagaggat gatgaggagg gtcacctgat ctgtcagagt ggagacgtac taagtgcaag 900
atgtatagaa tatttttcaa cacttattaa cttttcagat aacataatct atatatagat 960
taagctttca gggatttgga aatctttttt tctttctctt ttttgttttt gttttatttt 1020
tccatttctt ttggtggggg ggattgtatt tttgctttct ttagaaatgt aatgtttgtt 1080
atatagaact tccagaacag taatcaaatt aatgaaatta gacctataa ttatgttttt 1140
tgatggtggt gaccaataaa atatctagtg ataaggaaat ttgtagcatc aactagaata 1200
atctacattg atagcattta ttgtgataag tacattgttt ccacttcttg atatgactga 1260
gatttatttc tctcttttag atgaaattgt tgatacttta ggtgaaggag cttttggaaa 1320
agttgtggag tgcctcgatc ataaagcggg aggtagacat gtagcagtaa aaatagttaa 1380
aaatgtggat agatactgtg aagctgctcg ctcaaaaata caagtctctg aacatctgaa 1440
tacaacagac cccaacagta cttccgctg tgtccagatg ttggaatggt ttgagcatca 1500
tggtcacatt tgcattgtt ttgaactatt gggacttagt acttacgact tcattaaaga 1560
aaatggtttt ctaccatttc gactggatca tatcagaaag atggcatatc agatatgcaa 1620
gtctgtgaat tttttgcaca gtaataagtt gactcacaca gacttaaagc ctgaaaacat 1680
cttatttgtg cagtctgact acacagaggc gtataatccc aaaataaaac gtgatgaacg 1740
caccttaata aatccagata ttaaagttgt agactttggt agtgcaacat atgatgacga 1800
acatcacagt acattggtat ctacaagaca ttatagagca cctgaagtta ttttagccct 1860
aggggtggtc caaccatgtg atgtctggag cataggatgc attcttattg aatactatct 1920
tggtgttacc gtatttccaa cacacgatag taaggagcat ttagcaatga tggaaaggat 1980
tcttggaact ctacaaaac atatgatata gaaaaccagg aaacgtaaat attttcacca 2040
cgatcgatta gactgggatg aacacagttc tgccggcaga tatgtttcaa gacgctgtaa 2100
acctctgaag gaatttatgc tttctcaaga tgttgaacat gagcgtctct ttgacctcat 2160
tcagaaaatg ttggagtatg atccagccaa aagaattact ctcagagaag ccttaaagca 2220
tcctttctt gaccttctga agaaaagtat atagatctgt aattggacag ctctctcgaa 2280
gagactcttc agactgtatc agtctaattt ttaaatttta agttattttg tacagctttg 2340
taaatcttta acatttttat attgccatgt ttattttgtt tgggtaattt ggttcattaa 2400
gtacatagct aaggtaatga acatctttt cagtaattgt aaagtgattt attcagaata 2460
aattttttgt gcttatgaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaggg aggggg 2516

```

<210> 122

<211> 1139

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1053)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1124)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1125)

<223> n equals a,t,g, or c

<400> 122

```
gtggcgacag ggggtgggagc ggacccaggc cgggagcagg cgccgcccgc agtgagaacc 60
ggggccggag ccgggtgcgg atttgctggg gctgagtcgg gggcgcgcg gccctgacct 120
ctgccctctg acctctcccc tagcaggcga ccatggggaa cgtgttggt gccagctcgc 180
cgcccgcagg gccgccaccg ccgcctgcgc cggccctcgt ggggctgccg ccacctccgc 240
cctcgccgcc gggcttcacg ctgccgccgc tgggaggcag cctggggccc ggcaccagta 300
cgaktcgarg ttcggaacgg acccccgggg ctgcaaccgc cagcgccctca ggggcccgcg 360
aggatggggc ctggggctgc ctgcccacc cgggcacatt cgaggagtgc caccggaagt 420
gcaaggagct gtttccatt cagatggagg gtgtcaagct cacagtcaac aaagggttga 480
gtaaccattt tcagggtcaac cacacagtag ccctcagcac aatcggggag tccaactacc 540
acttcggggc cacatatgtg gggacaaagc agctgagtcc cacagaggcg ttccctgtac 600
tggtgggtga catggacaac agtggcagtc tcaacgctca ggtcattcac cagctggggc 660
ccggtctcag gtccaagatg gccatccaga ccagcagtc gaagtttgt aactggcagg 720
tggacgggga gtatcggggc tctgacttca cagcagccgt caccctgggg aaccagacg 780
tcctcgtagg ttcaggaatc ctctagatccc actacctcca gagcatcacg ccttgccctg 840
ccctgggtgg agagctggtc taccaccggc ggccctggaga ggagggcact gtcattgttc 900
tagctgggaa atacacattg aacaactggg tggcaacggg aacgttgggc caggcgggca 960
tgcacgcaac atactaccac aaagccagtg accagctgca ggtgggtgtg gagtttgagg 1020
ccagcacaag gwtgcaggac accagcgtct ccnttsggg accagcttgg aacttgccca 1080
agggccaacc tcytctttca aaggstctgt tgggataagc aaannggat tcgtggggg 1139
```

<210> 123

<211> 2114

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1966)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2039)

<223> n equals a,t,g, or c

<400> 123

```
accccgcgcg ccactcgctc gcgtcmgagg gaggagaaag tggcgagttc cggatccctg 60
cctagcgcg ccacaccttt actccagaga tcatggctgc cgaggatgtg gtggcgactg 120
gcgcccaccc aagcgatctg gagagcggcg ggctgctgca tgagattttc acgtcgccgc 180
tcaacctgct gctgcttggc ctctgcatct tcctgctcta caagatcgtg cgcggggacc 240
agccggcggc cagcgcgac agcgacgacg acgagccgcc ccctctgccc cgctcaagc 300
ggcgcgactt cacccccgc gagctgcggc gcttcgacgg cgtccaggac ccgcgcatc 360
tcatggccat caacggcaag gtgttcgatg tgaccaaagg ccgcaaattc tacgggcccc 420
aggggcccga tgggtctttt gctggaagag atgcatccag gggccttgcc acattttgcc 480
tggataagga agcactgaag gatgagtacg atgaccttcc tgacctcact gctgcccagc 540
aggagactct gagtgactgg gagtctcagt tcactttcaa gtatcatcac gtgggcaaac 600
```

```

tgctgaagga gggggaggag cccactgtgt actcagatga ggaagaacca aaagatgaga 660
gtgcccggaa aaatgattaa agcattcagt ggaagtatat ctatTTTTgt atTTTgcaa 720
atcatttgta acagtccact ctgtctttaa aacatagtga ttacaatatt tagaaagttt 780
tgagcacttg ctataagttt ttttaattaa atcactagtg acactaataa aattaacttc 840
ttagaatgca tgatgtgttt gtgtgtcaca aatccagaaa gtgaactgca gtgctgtaat 900
acacatgtta atactgtttt tcttctatct gtagttagta caggatgaat ttaaatgtgt 960
ttttcctgag agacaaggaa gacttgggta tttcccaaaa caggtaaaaa tcttaaatgt 1020
gcaccaagag caaaggatca acttttagtc atgatgttct gtaaagacaa caaatccctt 1080
tttttttctc aattgactta actgcatgat ttctgtttta tctacctcta aagcaaatct 1140
gcagtgttcc aaagactttg gtatggatta agcgtgttcc agtaacaaaa tgaaatctca 1200
aaacagagct cagctgcaaa aaagcatatt ttctgtgttt ctggactgca ctgttgcctt 1260
tgccctcaca tagacactca gacaccctca caaacacagt agtctatagt taggattaaa 1320
ataggatctg aacattcaaa agaaaagcttt ggaaaaaaag agctggctgg cctaaaaacc 1380
taaatatatg atgaagattg taggactgtc ttcccaagcc ccatgttcat ggtggggcaa 1440
tggttatTTg gtatttttac tcaattgggt actctcattt gaaatgaggg agggacatac 1500
agaataggaa cagggtgttg ctctcctaag agccttcattg cacaccctg aaccacgagg 1560
aaacagtaca gtcgctagtc aagtggtttt taaagtaaag tatattcata aggtaacagt 1620
tattctgttg ttataaaact ataccctctg caaaagtagt agtcaagtgt ctaggtcttt 1680
gatattgtc ttttggttaa cactaagctt aagtagacta tacagttgta tgaatttgta 1740
aaagtatatg aacacctagt gagatttcaa acttgtaatt gtgggttaa atgtcattgta 1800
ttttcttggt aactgtgttt tatgatttta cctcaaatca gaaaacaaaa tgatgtgctt 1860
tggtcagtta ataaaaatgg ttttaccac taaaaaaaaa aaaaaaaggg cgccgctct 1920
aaaggatccc tcgaggggcc caagcttacg cgtgcatgcy acgtcntagc tctctcccta 1980
tagtgagtcg tattataagc taggcactgg ccgtcgTTTT acaacgtcgt gactgggana 2040
tctgctagct tgggatcttt gtgaaggaac cttacttctg tgggtgtgaca taattggaca 2100
aactacctac agag 2114

```

&lt;210&gt; 124

&lt;211&gt; 583

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 124

```

gcccgcccta ttcccttggg cttttaaaaa gcgtcttTga tggaggtggg gcaggtgctc 60
accaagcccc cagtaacca agttgcatgt atccccaggg cacttttTgt attccccTgc 120
ttgtgactgc acaccgggac cccactcaat tcaaagaccc agactgcttc aaccctacca 180
acttcctgga caaggccaag ttccagggca atgatgcttt catgcccttt gcctcaggtg 240
caggcagagg aggaagggga ccagcctgga ctggctctgg ggtacctggg gctcactgtg 300
cacctgtgta cccggcaaag cagatgtgcc tgggcacagg cctggcccac tcgggtatct 360
tcctattcct tacggccacc ttacagaggt tctgcctgct ccctgtggta cgccctggca 420
ccatcaacct cacctgcagt gcaactggcct gggcagtgtc cccccagact tccagctcca 480
gccagtggcc tgctgaggtc aggtccact atggtgggct cactggccct caaacctcca 540
taccctccts ggtcaataaa ggccctaaat tgcaaaaaaa aaa 583

```

&lt;210&gt; 125

&lt;211&gt; 1987

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (7)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (14)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (517)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1960)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 125

```

cagtacngtc cgantcccgg gtcgacccac gcgtccgatg gcggcggagg aacctcagca 60
gcagaagcag gagccgctgg gcagcgactc cgaagtgtta actgtctggc ctatgatgaa 120
gccatcatgg ctcagcagga ccgaattcag caagagattg ctgtgcagaa ccctctggtg 180
tcagagcggc tggagctctc ggtcctatac aaggagtatg ctgaagatga caacatctat 240
caacagaaga tcaaggacct ccacaaaaag tactcgtaca tccgcaagac caggcctgac 300
ggcaactgtt tctatcgggc ttctcgattc tcccacttgg aggcactgct ggatgacagc 360
aaggagttgc agcggtgaga aggggtggga ctgggcaccg aggcaggtgg gtgtytacct 420
cctccccggg cgagtaggat gtgtctcgag taggggtgtc ycctccttcc cgggcgatgg 480
gctggactct ggccttgcca rgcggggcag tgctgtntcg gccctggcgt ctgggctggg 540
cgaggagccc atgctgggcc cgcccttcca tcccaccccc aggttcaagg ctgtgtctgc 600
caagagcaag gaagacctgg tgtcccaggg ctctactgaa ttcacaattg aggatttcca 660
caacacgttc atggacctga ttgagcaggt ggagaagcag acctctgtcg ccgacctgct 720
ggcctccttc aatgaccaga gcacctccga ctaccttgtg gtctacctgc ggctgctcac 780
ctcgggctac ctgcagcgcg agagcaagtt cttcgagcac ttcatcgagg gtggacggac 840
tgtcaaggag ttctgccagc aggaggtgga gcccatgtgc aaggagagcg accacatcca 900
catcattgcg ctggcccagg ccctcagcgt gtccatccag gtggagtaca tggaccgagg 960
cgagggcggc accaccaatc cgcacatctt ccctgagggc tccgagccca aggtctacct 1020
tctctaccgg cctggacact acgatatact ctacaaatag ggctggctcc agcccgtgc 1080
tgccctgctg ccccccctctg ccaggcgcta gacatgtaca gaggtttttc tgtggttgta 1140
aatggtccta tttcaccccc ttcttctctgt cacatgaccc ccccccctgt tttattaaag 1200
ggggtgctgg tggtagcccg tgtgtgcgtg tccctgctct gctgcccgcc tggctgctct 1260
gtctgctgcc ccctcccccc aggtgggtcc ccctgctttt cacctatcta ctccctgagct 1320
tccccaacag gagcagggtt gaggggccag gcctcttggg ggcccctcct gcttcgttgg 1380
gttctgcttc cttcccttct tagctggctc aggggcttct atgggacctt ggaagttcct 1440
tagggacttg cccagggtcc cagggccacc cacacttcat ctgctccctc ataggcccca 1500
cctccacgtc ccggctgggc ccagacccc agcttcctgc cctccaccgg gagtctgcat 1560
ggtttggagt cctgggtgga ggggcctttg tgaggctgga cccggctcag ggcaggtgga 1620
ggagctgggc ctcccacagg gtgcccgggc agtgccatcc tgggtgggga gggcagcctt 1680
caaacgtgtg gggctetamag tctcaggtc taggcagggc tgccggttct ccacctcccc 1740
atccgccccca ggccccctgc ctgtgcctgc cttgcacccc ctctgcttgg gccacgggtg 1800
ctctgcattg cctgcctttt tgcccttacc tcttttcttc cccgccccct gcacattcgg 1860
gktctcagcc cccaggctgt gagctccttg gggcaggccc tcaataaatg tgaaactgct 1920

```

gctgcaaaaa aaaaaaaaaa aaaaaaaggg ggccgcttan agatcctcaa gggccaagta 1980  
cggtgat 1987

<210> 126

<211> 1451

<212> DNA

<213> Homo sapiens

<400> 126

ggctgaccca cgcgtccgag atggcggagc gcgggtacag cttttcgtcg actacattca 60  
gcccgtctgg taaacttgct cagattgaat atgctttggc tgctgtagct ggaggagccc 120  
cgcccggtgg aattaaaagct gcaaatgggtg tggatttagc aactgagaaa aaacagaaat 180  
ccattctgta tgatgagcga agtgtacaca aagtagaacc aattaccaag catatagggt 240  
tggtgtacag tggcatgggc cccgattaca gagtgcctgt gcacagagct cgaaaactag 300  
ctcaacaata ctatcttggtg taccaagaac ccattcctac agctcagctg gtacagagag 360  
tagcttctgt gatgcaagaa tatactcagt cagggtggtgt tcgtccattt ggagtttctt 420  
tacttatttg tggttggaat gagggacgac catatttatt tcagtcagat ccatctggag 480  
cttactttgc ctggaaagct acagcaatgg gaaagaacta tgtgaatggg aagactttcc 540  
ttgagaaaag atataatgaa gatctggaac ttgaagatgc cattcataca gccatcttaa 600  
ccctaaagga aagctttgaa gggcaaatga cagaggataa catagaagtt ggaatctgca 660  
atgaagctgg atttaggagg cttactocaa ctgaagttaa ggattacttg gctgccatag 720  
cataacaatg aagtgactga aaaaatccaga atttcagata atctatctac ttaaactatg 780  
ttaaagtatg ttttggtttg cagacttttt gcatacttat ttctacatgg tttaaatcga 840  
ctgtttttta aatgacactt ataaatcccta ataaactgtt aaaccacact tccagccttt 900  
taggagttgc taaaatttta acagttattt ccygcttttt atcacagttg atttctgaag 960  
actayattgc caagcagaat gatgaaatga ctttttcggt gtcaggcaat tttggttaag 1020  
tcaaactcta atgccctctt cgctatcaga tgttgctgtg gtttcataa agcaaaatgc 1080  
tgatttttgg aaaaaacatg actgcttcta gagctgggag gatctgcaga ctttcacgga 1140  
ttcatggaac aagaaaagaa gcataggtac ttttaggtgc cattaggtat tgatcagtga 1200  
aatcctaggg tgctctatga gattgtacta ggcctatgaa gagtggtaag ccaaataggt 1260  
ctccatggga gatacattat gtaataaat aaacaatggt ttgctgggtc ctgttggtgt 1320  
ctccacaagt aggtaaacat gtttaagga acccggttc ttagattttg ttagactttt 1380  
taaactcaag gatgagcata agtgcttgaa ataaatgct aatacttaag tgtcaaaaaa 1440  
aaaaaaaaa a 1451

<210> 127

<211> 1234

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (857)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1204)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1226)

<223> n equals a,t,g, or c

<400> 127

```
aggttcccag ctagccagta aattcttttaa agacaagcat tgtacccttt gcctcagtgt 60
gccagacc aacctggcac atgctctatt catgttttcc atgagtgttt catgttagag 120
gtgtattttg tacacagggt ttatgctggg ggctcagaga gaagtggaca gcagattgtt 180
ggccctccca ggaagaaaag tcccaacgag ctggtgggat gatctcttta aagggtccaa 240
agagcatgga gctgtagctg tggagcgagt gaccaagagc cctggagaga ccagtaaacc 300
gagaccattt gcaggaggtg gctaccgcct tggggcagca ccagaggaag agtctgccta 360
tgtggcagga gaaaagaggc agcattccag ccaagatgtt catgtagtat tgaaactctg 420
gaagagtgga ttcagcctgg ataattggaga actcagaagc taccaagacc catccaatgc 480
ccagtttctg gactctatcc gcagagggga ggtgccagca gagcttcgga ggctagctca 540
cgggtggacag gtgaacttgg atatggagga ccatcgggac gaggactttg tgaagcccaa 600
aggagccttc aaagccttca ctggcgaggg tcagaaactg ggcagcactg ccccaggtg 660
ttgagtacca gctctccagc ccaacaggca gaaaatgaag ccaaagccag ctcttccatc 720
ttaatcgacg aatcagagcc taccacaaac atccaaattc ggcttgacga cggcgggagg 780
ctggtgcaga aatttaacca cagccacagg atcagcgaca tccgactctt catcgtggat 840
gcccggccag ccatggntgc caccagcttt atcctcatga ctactttccc gaacaaagag 900
ctggctgatg agagccagac cctgaaggaa gccaacctgc tcaatgctgt catcgtgcag 960
cggttaacat aaccgcccag ccagctgcct ggctccctc ctgtgtttcc catggccagt 1020
ggccatgcc catggggatc gcccctcctg ccccttctg caccaccagc agtccagtgc 1080
aacgtctcct ccatagctct gggttcttag atcttggttg gacgtttgtt ttctccttag 1140
ttgcatttcc tgggtttttg tgatgatcaa tggactttta tgaaaaaaa aataaaaaa 1200
accnaaaggg gggcccgtc ccaatncccc cctt 1234
```

<210> 128

<211> 863

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (840)

<223> n equals a,t,g, or c

<400> 128

```
cccacgcgtc cgcaggcgcg ctccggctgc cgctggctct tcgcacgcgg ccatggccga 60
ctccgagctg cagctggttg agcagcggat ccgcagcttc cccgacttcc ccaccccagg 120
cgtggtattc agggacatct cgcccgctct gaaggacccc gcctccttcc gcgcccgcct 180
cggcctcctg gcgcgacacc tgaaggcgac ccacgggggc cgcacgcact acatcgagg 240
cctagactcc cgaggcttcc tctttggccc ctccctggcc caggagcttg gactgggctg 300
cgtgctcatc cgaaagcggg ggaagctgcc agggcccact ctgtgggcct cctattccct 360
ggagtacggg aaggctgagc tggagattca gaaagacgcc ctggagccag gacagagggg 420
ggtcgtcgtg gatgatctgc tggccactgg tggaccatg aacgctgcct gtgagctgct 480
gggcgcgctg cagctgagg tcttgagtg cgtgagcctg gtggagctga cctcgcttaa 540
gggcaggag aagctggcac ctgtaccctt cttctctctc ctgcagtatg agtgaccaca 600
gggcctccca gcccaacatc tccagctgga tcccaggga atatcagcct tgggcaactg 660
cagtgaccag gggcaccggc tgcccacagg gaacacattc ctttgctggg gttcagcgcc 720
tctcctgggg ctggaagtgc caaagcctgg ggcaaagctg tgtttcagcc aactgaacc 780
```

caattacaca cagcgggaga acgcagtaaa cagctttccc acaaaaaaaaa aaaaaaaaaan 840  
aaaaaaaaaa aaaaagggcg gcc 863

<210> 129

<211> 1238

<212> DNA

<213> Homo sapiens

<400> 129

cacagtgtct gctgtgattg agatgcgcac aggttggggg aggtagggcc ttacgcttgt 60  
cctcagtgagg ggcagtttgc cttagatgac arctgggctc ttcttcacac cacctgcagc 120  
ccctccctgc ccctgcccta gctgctgtgt gtccagttgc cttctttcta cctcagccgg 180  
cgtggagtggt tctctgtgca gttagtgcc cccacacac ccgtctcttg attgagatgt 240  
ttctgggtgt tatgggttcc ccgtggagct kgggggtggg gccgtgtacc taagctggag 300  
gctggcgctc tccctcagca caggtgggtc agtggccagc aggccatct ggagtgggag 360  
tgggcacttc caccgcgc acaggccatc cggctgtgca ggccagcccc taggagcarg 420  
tcccgggtga ctggcagttt tcacggtcta gggccgagac gatggcatgg ggcctagagc 480  
atgaggtaga gcagaatgca gaccacgccg ctggatgccg agagaccctg ctctccgagg 540  
gaggcatctg tgtcatgctg tgagggtgga ggacggggcc ctagtctctg gttttcttgt 600  
cttaacatcc ttatctgtgt ccgccacgga ggtgactgag ctgctagcga gttgtcctgt 660  
cccaggtact tgagtttttg aaaagctgac tcacgcccac ccatctcaca gcccttccct 720  
ggggacagtc gcttccgcct tgacacctca ctctcagttg aataactcaa gcttgggtcat 780  
cttcagactc gaattcttga gtagaccacg acggcttagc ccaagtctag ttgcagctgc 840  
ctcggcaagt cccatttgc tcaggcagcc ctgaatggg ctgtttacag gaatggtaaa 900  
ttgggatttg aaggaatata gcttccagct tcataggcta gggtgaccac ggcttaggaa 960  
acagggaaaag aaagcaaggc ctttttccct cctttcccgg gatctgtcta ctccacctcc 1020  
acgggggagg ccagtgggga agggctgtca cctcttcccc atctgcatga gttctggaac 1080  
tctgtcctgt tggctgcttg cttccagctc cccccaatct ccacgcagc gggttcctcc 1140  
tgtcttttct acagtgtcat aaaacatcct gccctaccc tctcccaaag gtcaatttta 1200  
attctyawca agaagattta tgaggagaag aaaaagaa 1238

<210> 130

<211> 379

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (373)

<223> n equals a,t,g, or c

<400> 130

tggtttggga gctgccaggc tcctgggagg atcgcagtc gcagagcagg gctgaggcct 60  
gggggttagga gcagagcctg cscatctgga ggcagcatgt ccaagaaagg gaggtaggt 120  
gcagcraagg acccaggggc agagccacgc tggggatgga ccccttcag gacacgctgc 180  
ggyggctgcg tgaggccttc aactgagggc gcacgcggcc ggccgagttc cgggctgcgc 240  
actccagggc ctgggccaact tccttcaaga aaacaagcar cttctrcgm acgtgctggc 300  
ccaggaaactg cataagccag ctttcgaagg cagacatata tgagtcatcc ttgcccagaa 360  
cgaggttgaa tangctctt 379

<210> 131



&lt;211&gt; 1786

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 131

```
cctgggcgct aagatggcgg cggcgtgagt tgcattgtgt gtgaggatcc cggggccgcc 60
gcgtcgctcg ggccccgcca tggccgtcac catcacgctc aaaacgctgc agcagcagac 120
cttcaagatc cgcattggagc ctgacgagac ggtgaagggtg ctaaaggaga agatagaagc 180
tgagaagggt cgtgatgcct tccccgtggc tggacagaaa ctcatctatg ccggcaagat 240
cttgagtgac gatgtcccta tcagggacta tcgcatcgat gagaagaact ttgtggtcgt 300
catggtgacc aagaccaaag ccggccaggg tacctcagca cccccagagg cctcaccac 360
agctgcccc aagtcctcta catccttccc gcctgcccc acctcaggca tgtcccatcc 420
cccacctgcc gccagagagg acaagagccc atcagaggaa tccgccccca cgacgtcccc 480
agagtctgtg tcaggctctg ttccctcttc aggttagcagc gggcgagagg aagacgcggc 540
ctccacgcta gtgacgggct ctgagtatga gacgatgctg acggagatca tgtccatggg 600
ctatgagcga gagcgggtcg tggccgccct gagagccagc tacaacaacc cccaccgagc 660
cgtggagtat ctgctcacgg gaattcctgg gagccccgag ccggaacacg gttctgtcca 720
ggagagccag gtatcggagc agccggccac ggaagcagga gagaaccccc tggagtccct 780
gcgggaccag cccagttcc agaactgagc gcaggtgatt cagcagaacc ctgcgtgct 840
gcccgcctg ctccagcagc tgggcccagga gaacctcagc cttttacagc aaatcagccg 900
gcaccaggag cagttcatcc agatgctgaa cgagccccct ggggagctgg cggacatctc 960
agatgtggag ggggaggtgg gcgccatagg agaggaggcc ccgcagatga actacatcca 1020
ggtgacgccg caggagaaaag aagctataga gaggttgaag gccctgggct tcccagagag 1080
cctggtcatc caggcctatt tcgctgtgta aaaaaatgag aacttggctg ccaacttcct 1140
cctgagtcag aactttgatg acgagtgatg ccaggaagcc aggccaccga agccccacc 1200
ctacccttat tccatgaaaag ttttataaaa gaaaaaatat atatataatc atgtttattt 1260
aagaaatgga aaaaaaatc aaaaaatcta aaaaaacaag caaacagtcc agcttcctgt 1320
cctcctaaag tggccccgtg tcccatctcc cgggccagac agctgtcccc ccgtcctcct 1380
ccccagccca gcctgctcag agaagctggc aggactggga ggcgacagat ggccccctct 1440
tggcctctgt cccagctctc tgcagccaga cggaaaggcg gctgcttgcc tctccatcct 1500
ccgaaaaacc cctgaggacc ccccccatc ctcttctagg atgaggggaa gctggagccc 1560
caactttgat cctccattgg agtggcccaa atctttccat ctagggcaag tcctgaaagc 1620
ccaaggcccc ctccccagtc tggccttgcc tccagcctgg agaagggcta acatcagctc 1680
attgtcaagg ccacccccac ccagaaacag aaccgtgtct ctgataaagg ttttgaagtg 1740
aataaagttt taaaaactaa aaaaaaaaaa aaaaaaaaaa aaaaaa 1786
```

&lt;210&gt; 132

&lt;211&gt; 974

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (165)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (853)

&lt;223&gt; n equals a,t,g, or c

<220>

<221> misc feature

<222> (963)

<223> n equals a,t,g, or c

<400> 132

```
ggcagctaac ctcctcatcc ccgctgtggg ttctagcctc tctgaagccc tggacttgat 60
cgagtcggac cctgatgctt ggtgtgacct gagtaaattt gacctccctg aggaaccatc 120
tgcagaggac agtatcaaca acagcctagt gcagctgcaa gcgtncacat cagcagcaag 180
tcctgccacc ccgccagcct tccgccctgg tgcccagtggt gaccgagtag cgccctggatg 240
gccacaccat ctacagacct agccggagca gccggggcga gctgatcccc atctccccc 300
gcactgaagt cgggggctct ggcattggca caccgccctc tgtgtctcaag cggcagagga 360
agaggcgtgt ggctctgtcc cctgtcactg agaatagcac cagtctgtcc ttccctggatt 420
cctgtaacag cctcacgccc aagagcacac ctgttaagac cctgcccttc tcgccctccc 480
agtttctgaa cttctggaac aaacaggaca cattggagct ggagagcccc tcgctgacat 540
ccaccccagt gtgcagccag aaggtggtgg tcaccacacc actgcaccgg gacaagacac 600
ccctgcacca gaaacatgct gcgtttgtaa cccagatca gaagtactcc atggacaaca 660
ctccccacac gccaaacccg ttcaagaacg ccctggagaa gtacggaccc ctgaagcccc 720
tgccacagac cccgcacctg gaggaggact tgaaggaggt gctgcgttct gaggctggca 780
tcgaactcat catcaggagc gacatcaggc ccgagaagca gaagaggaag cctgggctgc 840
ggcggagccc atncaagaaa gtccggaagt ctctggctct tgacattgtg gatgaggatg 900
tgaagytgat gatgtccaca ytgcccaakt ytttatcctt ggcgacaayt gcccttgca 960
aanttttcca gcct 974
```

<210> 133

<211> 634

<212> DNA

<213> Homo sapiens

<400> 133

```
attcggcacg acgggtgaac ctggccacag ctcaccctgg aacagccaca atgtctgccc 60
cttagagaag aaccctgaaa tcagaccagt ttttgcgccc tcccccttc ctctctgtta 120
cagtgccttt tccaggcctt aagagaagta aaacttagct gcagcgtcag gaggtggacc 180
ccagagtgtg agtggcacgc ttctctgtga acccgctcctc accatgtttg ccacatctgg 240
ggcagtgcca gcggggaagc cttactctgt cagcgaatgt ggcaagagct tctgctacag 300
ctcagtgtct ctgcgacatg aacgagctca cggcggtgac ggccgcttcc gttgcctaga 360
atgcggtgag cgctgtgcac gggctgtgta cctccgagcg cacaggcgca cgcattgtgg 420
ccagaccctc tacatctgca gtgagtgcgg acaaagcttc cgccacagcg gccgtcttga 480
cctacacttg ggcgcacacc ggcagcgatg ccgcacttgc ccctgccgca cwtgcgggcg 540
gcgcttcccg cacttcccgg cgctgtgtct acaccggcgc cgccagcatc tgccagagcg 600
gccccgscgy tgcccgctgt gcgycctcag gttt 634
```

<210> 134

<211> 1855

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1818)

<223> n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1845)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 134

```
gcccacgcgt cccgcggcgc gcccgagggc gccgcgtgcg gcctgcagga gggcccgtgc 60
ggcgaggggc tgcagtgcgt ggtgcccttc ggggtgccag cctcgccac ggtgcggcgg 120
cgcgcgaggg cccgcctctg tgtgtgcgcc acagcgagcc ggtgtgcggc agcgacgcca 180
acacctacgc caacctgtgc cagctgcgcg ccgccagccg ccgctccgag aggctgcacc 240
ggccgcgggt catcgtcctg cagcgcgagg cctgcggcca agggcaggaa gatcccaaca 300
gtttgcgcca taaatataac ttatcgcgg acgtggtgga gaagatcgcc cctgccgtgg 360
ttcatatcga attgtttcgc aagcttccgt tttctaaacg agaggtgccg gtggctagtg 420
ggtctgggtt tattgtgtcg gaagatggac tgatcgtgac aaatgcccac gtggtgacca 480
acaagcaccg ggtcaaagtt gagctgaaga acggtgccac ttacgaagcc aaaatcaagg 540
atgtggatga gaaagcagac atcgactca tcaaaattga ccaccagggc aagctgcctg 600
tcctgctgct tggccgctcc tcagagctgc gcccgggaga gttcgtggtc gccatcgaa 660
gcccgtttcc ccttcaaaac acagtcacca ccggggtcgt gagcaccacc cagcgaggcg 720
gcaaagagct ggggtcctcg aactcagaca tggactacat ccagaccgac gccatcata 780
actatgaaa ctcgggaggc ccgttagtaa acctggacgg tgaagtgatt ggaattaaca 840
ctttgaaagt gacagctgga atctccttt caatcccatc tgataagatt aaaaagttcc 900
tcacggagtc ccatgaccga caggccaaag gaaaagccat caccaagaag aagtatattg 960
gtatccgaat gatgtcactc acgtccagca aagccaaaga gctgaaggac cggcaccggg 1020
acttcccaga cgtgatctca ggagcgtata taattgaagt aattcctgat accccagcag 1080
aagctggtgg tctcaaggaa aacgacgtca taatcagcat caatggacag tccgtggtct 1140
ccgccaatga tgtcagcgac gtcattaaaa gggaaaagcac cctgaacatg gtggtccgca 1200
gggtaatgaa gatcatcatga tcacagtgat tcccgaagaa attgacccat aggcagaggc 1260
atgagctgga cttcatgttt ccctcaaaga ctctcccggt gatgacggat gaggactctg 1320
ggctgctgga ataggacact caagactttt gactgccatt ttgtttgttc agtggagact 1380
ccctggccaa cagaatcctt cttgatagtt tgcaggcaaa acaaatgtaa tgttgagat 1440
ccgcaggcag aagctctgcc cttctgtatc ctatgtatgc agtgtgcttt ttcttgccag 1500
cttgggccaat tcttgcttag acagtcagca tttgtctcct cctttaactg agtcatcatc 1560
ttagtccaac taatgcagtc gatacaatgc gtatagatga gaagcccac gggagccagg 1620
atgggactgg tcgtgtttgt gcttttctcc aagtcagcac ccaaaggcca atgcacagag 1680
accccggtg ggtgagcgct ggcttctcaa acggccgaag ttgcctcttt taggaatctc 1740
tttggaattg ggagcacgat gactctgagt ttgagctatt aaagtacttc ttacacattg 1800
aaaaaaaaa aaaaaaanct cggggggggg cccggtaccc aattngcctt ttaag 1855
```

&lt;210&gt; 135

&lt;211&gt; 917

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (913)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 135

```
ggttttttgc gcgtgcatat ggcggtggcg ggtgggggga agggggagat cctgctgcac 60
```

```

tggccgcccc agttgggggg cgagctcggt ggtgacgcgc ggccctcacg tgacccarag 120
ctgcagagcg acgcagcctt cggtgcagtc gtcactcgcg tctggctacc agtccccgc 180
tgccctgagc tcggcgggct ggcattcggc ccggggaaaa gcggagcagg tctgcgaggc 240
taagtgtctc cgcgcgccac ctgcggcgga gaatccggag gagaaggaga ctgcaaggat 300
agggccagga aaacgaagag atggagcagc ctatgcagaa tggagaggaa gaccgccctt 360
tggaaggagg tgaaggccac cagcctgcag gaaatcgacg gggacaggct cgccgacttg 420
cccctaattt tcgatgggcc ataccctaata ggcagatcaa tgatgggatg ggtggagatg 480
gagatgatat ggaaatattc atggaggaga tgagagaaat cagaagaaaa cttagggagc 540
tgcagttgag gaattgtctg cgtatcctta tgggggagct ctctaatac catgaccatc 600
atgatgaatt ttgccttatg ccttgactcc tgccatttat catgagatta atactgtgat 660
tcccgtggtt ttctttttcc ttgcattttc ctaatatgcc ttactgatc cgtttgctgt 720
gaaccctatg ttatttccat gtgtcaagtg ggtcttgtgt tgccagcttc tatttgaaga 780
ttgcctttgc actcagtgtg agtttctgtc agcagtagtt tcacccattt gcatggaaaa 840
atttaaagct aataaagcaa tttaaaaagc aaaaaaaaaa aaaaaaaaaa aaaaaamamg 900
ggggggcccg gwnccca 917

```

<210> 136

<211> 1271

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1236)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1255)

<223> n equals a,t,g, or c

<400> 136

```

gcaaggcttc ccctctaccc tctctgggcc tctcacaaac gctgagcccc gccccgctga 60
ggcctgtctg cagaatccac ascaaccagc accatgcccc tgayactggg gtactggrac 120
atccgcgggc tggccaykc catccgcctg ctccctggaat acacagactc aagctaygag 180
gaaaagaagt acacgatggg ggacgctcct gattatgaca gaagccagtg gctgaatgaa 240
aaattcaagc tgggcctgga ctttcccaat ctgccctact tgattgatgg grctcacaag 300
atcacccaga gcaacgccat cctgcggtac attgcccga agcacaacct gtgcggggaa 360
tcagaaaagg agcagattcg cgaagacatt ttggagaacc agtttatgga cagccgtatg 420
cagctggcca aactctgcta tgaccagat tttgagaaac tgaaaccaga atacctgcag 480
gcactccctg aaatgctgaa gctctactca cagtttctgg ggaagcagcc atggtttctt 540
ggggacaaga tcacctttgt ggatttcatc gcttatgatg tccttgagag aaaccaagta 600
tttgagccca gctgcctgga tgccttccca aacctgaagg acttcatctc ccgatttgag 660
ggcttgagga agatctctgc ctacatgaag tccagccgct tcctcccaag acctgtgttc 720
acaaagatgg ctgtctgggg caacaagtag ggccctgaag gccaggaggt gggagtggag 780
agcccatact cagcctgtcg ccaggtgtg gcagcgcagc tggactctgc atccagcac 840
ctgcctcctc gttcctttct cctgtttatt cccatcttta ctcccaagac ttcattgtcc 900
ctcttcactc cccctaaacc cctgtcccat tgaggccctt tgaagcctca gctaccact 960
atccttcgtg aacatccct cccatcatta cccttcctg cactaaagcc agcctgacct 1020
tccttcctgt tagtggttgt gtctgtttaa aargcctgcc tggccctcg cctgtggagc 1080
tcagcccccga gctgtccccg tggtgcatga aggagcagca ttgactggtt tacaggccct 1140

```

gctcctgcag catgggtccct gccttaggcc tacctgatgg aagtaaagcc tcaaccacaa 1200  
aaaaaaaaaa aaaaaatttg ggggggggcc cggtanccca tttggccctt taggnngggg 1260  
ggttttaaat t 1271

<210> 137

<211> 2017

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (295)

<223> n equals a,t,g, or c

<400> 137

ggaatgtcat cagtgttgac ccgaatgatc agaaaaagac agcttggtat gacattgatg 60  
ttgaagtgga tgacaccttg aagaccaga tgaattcttt tctgctgtcc actgccagcc 120  
aacaggagat tgctactcta gacaacaaga caatgactga tgtggtgggt aaccararga 180  
rgagcgccga gctgagttct acttccagcc ctgggkcagg aggctgtgtg ccratacttc 240  
tactccaagg tgcagcagag acgacaagaa ttagagcaag ccctgggaat ccggnataca 300  
tagggcctct cccacagccc tgattcgact gcaccaattc ttgawttggg ccctgtgctg 360  
cctgcctcat agtatctgcc ttggtcttgc ttggggcggt ccaggggatg ctgttggttc 420  
aaggacaaca ccagaatgaa gagggctcga caagacacct gttatcctct tcttccacc 480  
tatctcttcc cacccccagc ttccctttgc cccacaaaagt tcccatgtgc ctgtaccctc 540  
ccctggtcta cataggacct ctagatagtg ttagagagag aacatgtagt ggtaatgagt 600  
gcttggaatg gattgggcct caggccaggt ggtcttcaag gggaccagct aactgatcct 660  
gcccttcaga gaccaggag ttgggagctt tcgctccttc tccaagactc aggcctgtgg 720  
gactctata agctagtga tcttggtctc cctgataaca gaatccaatt tccttccctc 780  
cctccacagg tttggaacaa actctccctt cacttggtgc cctgtagcac tacagaaacc 840  
ctgggtcttg ggctccactg gccccagggg cagtcgccag ccctctgggt tgrcctgctg 900  
tcagtgtctc tytactcct tagttggggg ccacatcagt attggagttt tgttctttat 960  
tgctccctcc cagacactcc ctgtggctgc cctttgtgat tccctcagat ctgccctaatt 1020  
cccgggcatt tgggtggggg aatcttgctt tccctttca gagccccagg gatctcatct 1080  
ggggaactgt cattgccagc agaggctgtt ccttctgct gtttgagat gtgactcatt 1140  
cattcactca ctccaccctg cctctgcac ccttaatgga gaaacgggcc taaaacaaa 1200  
cgggtaaaaa gccctgggcc atccctgtct tccgtccct tgtctgccc gttgacacct 1260  
actggtgact tctaggcac tgaggagtga aagcgctag ggctggagaa tagcgtgag 1320  
ttgggtttgt gactcttccc tctccctgcc tcacaggatt gtgactcccc agccctgcc 1380  
ctcaaagctt cagaccctc aggtagcagc aggacctgt gatcttggcc ccttgatct 1440  
gagatggttt ttgcacttt ccaggagagc ctcacattct tcttccaggt tgtatcacc 1500  
ccgagttagc atatcccagg ctgcagact caacacagca agggtagggg acagctgggc 1560  
acaaaggggg aattccgttc agcatgggct ctaaaccac agaactgaca aagccctgc 1620  
ttccccacc cctcctcagg ctccctgcag cacacccca ccccaaatc cctccctgtt 1680  
ctacactggg gacagcagaa ttttctccc gtcttccct tccctgccatt ttccctccct 1740  
tgaaaggttg aactggaca accttggggc agctgagccc tggccgctc ctggttgga 1800  
ccatgagaag gaagctcagt acttcccaca gtgtccctgt tgataactgt ttttattaac 1860  
tgaattgttt tttcatgga ccaaactttt tttgtactg tcccttatt gatgttacc 1920  
agttttaata aaagaatctt ctgaaggatg ggtcctccta cctactgtga gagagctctt 1980  
ccctgagctc ttcttcttc aataccatta aaaaaa 2017

<210> 138

<211> 937  
<212> DNA  
<213> Homo sapiens

<400> 138  
gattcaaaca ggcaacaatg acctttttatt ttctgtttgt cccacacctc ccagccttcc 60  
acctcctggt cttcctacct tcttcctttt tgactaaata atccccacct cccttgatca 120  
tacagtgagg ctacagtgac tgaggggaga atccctcctg ttcactctcc caaccctgct 180  
ccagcccctc agcttcccag accctcatgc agttggttgt aaattctccc aggagctggt 240  
ttactgtcta cttttcagga ttaaaaaaaaa aatcaaaact taaaaaaaa aaagttaaa 300  
aagcaaaatg gggaggggga ggaagcagtg actttttttt ggtaattatg cgcttttttt 360  
taatttttag aatttgtctt tttactgtgg gtgggctggt gatatttcat caagataagc 420  
atcttcttcc tgagttcagg tgactgagga agagccacaa aacaaaacac aacaaaacca 480  
aaccacagaa tcattctttaa cccaactttt tatacgatgc ccagttccc cataactttg 540  
cacacaagct tctgtgttca gttgaattgt aactgctttt tgtatttgga gagagtgact 600  
attgaacttg aaacctttta ttccgggcgt cttggtagt tctggtggga ttcagtgggt 660  
gagagggaag aaggggaggt tggggggctc cttcccttca gaacttgaag tttctccac 720  
tgccctcctc ccagtggtct cccaggtgcc agacccaaaa gcttttccta cagtataacc 780  
ctttattttt acttcccctt gactcatatg ttttaacatg attttaacaa actgcactta 840  
ttaagaaatg tgtttgccct gttttgtttg gtttcgtttt gttttctttg aataaatgac 900  
atggcacctc ctagcaggaa ggaaaaaaaa aaaaaaa 937

<210> 139  
<211> 2759  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (171)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1654)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2743)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2744)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2746)  
<223> n equals a,t,g, or c

&lt;400&gt; 139

gctagtctca caggaaccca ggcgttgccc ccactcttct ccctcggcta ccaccagagc 60  
cggttggaact accgggacga ggctgatgtg ctggaagtgg atcagggcct tgatgatcac 120  
aacctgccct gtgatgtcat ctggctagac attgaacatg ctgatggcaa ncgggtatttc 180  
acctgggacc ccagtcgctt ccctcagccc ygcaccatgc ttgascgctt ggcttctaag 240  
aggcsraagc tgggtggccat cgtagacccc cacatcaagg tggactccgg ctaccgagtt 300  
cacgaggagc tgcggaacct ggggctgtat gtwaaaaccc gggatggctc tractatrag 360  
ggctgggtct ggcagggctc agctgggttac cctgacttca ctaatccac gatgagggcc 420  
tggtgggcta acatgttcag ctatgacaat tatgagggtc cagctcccaa cctctttgtc 480  
tggaatgaca tgaacgaacc atctgtgttc aatggctctg aggtcaccat gctcaaggat 540  
gcccagcatt atgggggctg ggagcaccgg gatgtgcata acatctatgg cctttatgtg 600  
cacatggcga ctgctgatgg gctgagacag cgctctgggg gcatggaacg cccctttgtc 660  
ctggccaggg ccttcttcgc tggctcccag cgctttggag ccgtgtggac aggggacaac 720  
actgccagat gggaccattt gaagatctct attcctatgt gtctcagctt ggggctgggtg 780  
ggactttcct tctgtggggc ggatgtgggt ggcttcttca aaaaccaga gccagagctg 840  
cttgtgcgct ggtaccagat ggggtgcttac cagccattct tccgggcaca tgcccacttg 900  
gacactgggc gacgagagcc atggctgtta ccctctcagc acaatgatat aatccgagat 960  
gccttgggccc agcgatatct tttgctgccc ttctgggtaca cctcttata tcaggccccat 1020  
cgggaaggca tcctgtcat gagggccctg tgggtgcagt accctcagga tgtgactacc 1080  
ttcaatatag atgatcagta cttgcttggg gatgcgttgc tggttcaccg tgtatcagac 1140  
tctggagccc atggtgtcca ggtctatctg cctggccaag gggaggtgtg gtatgacatt 1200  
caaagctacc agaagcatca tggctcccag accctgtacc tgctgtaac tctaagcagt 1260  
atccctgtgt tccagcgtgg agggacaatc gtgcctcgat ggatgcgagt gcggcggtct 1320  
tcagaatgta tgaaggatga ccccatcact ctctttgttg cacttagccc tcagggtaca 1380  
gctcaaggag agctctttct ggatgatggg cacacgttca actatcagac tcgccaagag 1440  
ttcctgtctg gtcgattctc attctctggc aacacccttg tctccagctc agcagaccct 1500  
gaaggacact ttgagacacc aatctggatt gagcgggtgg tgataatagg ggctggaaag 1560  
ccagcagctg tgggtactcca gacaaaagga tctccagaaa gccgcctgtc cttccagcat 1620  
gaccctgaga cctctgtgtt ggtcctgcgc aagncctggca tcaatgtggc atctgattgg 1680  
agtattcacc tgcgataacc caaggatgt tctgggttag ggggagggaa ggggagcatt 1740  
agtgtgaga gatattcttt cttctgcctt ggagttcggc cctccccaga cttcacttat 1800  
gctagtctaa gaccagatt ctgccaacat ttgggcagga tgagagggct gaccctgggc 1860  
tccaaattcc tcttgtgatc tctcaccctc tcccactcca ttgataccaa ctctttccct 1920  
tcattcccc aacatcctgt tgctctaact ggagcacatt cacttacgaa caccaggaaa 1980  
ccacagggcc cttgtcggcc cttctcttcc cttatttag gagccctgaa ctccccaga 2040  
gtctatccat tcatgcctct tgtatgttga tgccacttct tggaagaaga tgagggcaat 2100  
gagttagggc tccttttccc cttccctccc accagattgc tctccacct ttcatttctt 2160  
cctccaggct ttactccct ttttatgccc caccgataca ctgggaccac cccttaccct 2220  
ggacaggatg aatggatcaa aggagtggag ttgctaaaga acatcctttt ccctctcatt 2280  
ctaccctttt cctctccccg attccttgta gagctgctgc aattcttaga ggggcagttc 2340  
tacctcctct gtccctcggc agaaagacgt ttccacacct cttaggggat gcgcattaaa 2400  
cttcttttgc ccccttcttg tccccttga ggggcactta agatggagaa atcagttgtg 2460  
gtttcagtg atcatgtca cctgtattta ttgctaggag aagcctgagg gtggggggag 2520  
atgatcatgt gtgctcgggg ttggctggaa gccctgggtg gggggttggg ggaggactaa 2580  
tggggagtcg gggaatattt gtgggtattt tttttacttc ctcttggttc ccagctgtga 2640  
cacgttttga tcaaaggaga aacaataaag ggataaacca taaaaaaaaa aaaaaaaaaa 2700  
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aannanaaaa aaaaataaa 2759

&lt;210&gt; 140

&lt;211&gt; 1241

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (317)

<223> n equals a,t,g, or c

<400> 140

```
tcgacccacg cgtccgggag aacgggcgga gggcgcgggc cgaccgggag caccgaccat 60
ggcctccaaa tgccccaagt gcgacaagac cgtgtacttc gccgagaagg tgagctccct 120
ggggaaggac tggcacaagt tctgcctcaa gtgcgagcgc tgcagcaaga cgctgacgcc 180
cgggggccac gccgagcatg acgggaagcc gttctgccac aagccgtgct acgccaccct 240
gttcggaccc aaaggcgtga acatcggggg cgcgggctcc tacatctacg agaagcccct 300
ggcggagggg ccgcagntca ccggcccat cgagggtccc gcggcccgag cagaggagcg 360
gaaggcgagc ggcccccgga aggscccagc agagcctcca gtgtcaccac tttcaccggg 420
gagcccaaca cgtgcccgcg ctgcagcaag aaggtgtact tcgctgagaa ggtgacgtct 480
ctgggcaagg attggcaccg gccctgctg cgctgcgagc gctgcgggaa gacactgacc 540
ccggcggggc acgcggagca cgacggccag ccctactgcc acaagccctg ctatggaatc 600
ctcttcggac ccaaggaggt gaacaccggt gcggtgggca gctacatcta tgaccgggac 660
cccgaaggca aggtccagcc ctaggctaca gcggctctca tgatgtgggc tcacctgcgc 720
cccagaccct gcaggggccc ccctgcttgg ctctgctggg agagtgtca gccgccaggt 780
cctgcctgca agcccagggc gagtattgga ggaggggcag ccacgggcag agcaccatgc 840
ccatccccga gtctctggtg tgtctgcccc ctctggcatc ctctggcggt cccatgatcc 900
cttctgtgtc tgcgtgtccg aatccccgtg tgaccctgtc ccagcathtt cccgccgacc 960
ctgctgttcc ccgtggcgct gtccgctctc cctctcctgc tgcccaccca cctgccagt 1020
ttatttatgc tcccttcgtg ggtgatggcc acgccctcac catgtccctg gcagagggct 1080
tcctccggga tccctgcct ggtgcccaca ctgctcgca agcgtcgcc accctcacgt 1140
ggctcacctg ctgttgagcc ttgtgctgtc aataaacggt ttgaggattg caaaaaaaaa 1200
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa g 1241
```

<210> 141

<211> 3405

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1569)

<223> n equals a,t,g, or c

<400> 141

```
cctttccgat acgtcctaga cccacctgcc cgccggatct ggaataatgt gactcgctgg 60
tttgtcacgt gtgtccggca gccagaattc cgagccgtgc taggagaagt ggttctatac 120
tcaggagcca ggctctctc tcatcagcca ggccccgagg ctccctgccct cccaaagaca 180
gtgctcagc tcaagaaaga ggcaaaagaa cgggagaagc tagagaaatt ccaacagaag 240
cagaagatcc aacagcagca gccacctyca ggggagaaga aaccaaacc agagaagagg 300
gagaaacggg rtyctgggt cattamctwt gacytcccaa ccccamccgg ggaaaagaaa 360
gatgtcagtg gcccctagcc cgactcctac agccctcggt atgtggaggc tgcctgttac 420
ccttggtggg agcagcaggg cttcttcaag ccagagtatg ggcgtcctaa tgtgtcagca 480
gcaaatcccc gaggtgtctt catgatgtgc atcccacccc ccaatgtrac aggctccctg 540
```



cacctgggmc atgcactcac caacgccatc caggactccc tgactcgatg gcaccgcatg 600  
cgtggggaga ccacctgtg gaacctggc tgtgaccatg caggtattgc caccaggtg 660  
gtgggtggaga agaagctatg gcgtgagmag ggactgagcc ggcaccagct gggccgcgag 720  
gctttctaca ggaagtctg aagtggagg aggagaaagg tgaccggatt taccaccagt 780  
tgaagaagct tggcagctcc ttggactggg atcgagcctg tttcaccatg gaccctaaac 840  
tctcagcagc tgtgacagag gcctttgtcc ggcttcacga ggaaggcatc atctatcgca 900  
gtacccgcct tgtaactgg tcctgcaccc tcaactccgc catctctgac attgaggtgg 960  
ataagaagga gctgacaggt cgcacctgc tctccgtgcc tggctacaag gagaaggtgg 1020  
agttcggggg cctcgtgtcc tttgcctata aggtccaagg ctcatatgc gacgaggagg 1080  
tggtggtggc aacaactcgg atcgagacaa tgctgggaga tgtggctgta gctgtgcacc 1140  
ccaaagatac cagataccag cacctgaagg ggaagaacgt gatccacca ttctgtctc 1200  
ggagccttcc cattgtcttc gatgaatttg tggacatgga ctttggcaca ggtgctgtga 1260  
agatcacccc cgcacatgac caaatgact atgaagttgg gcagcggcac gggctggagg 1320  
ccatcagcat catggactcc cggggggccc tcatcaatgt gcctccgcct tlyctggggc 1380  
tgcccagggt tgaggccagg aaagcgggtg tgggtggcgt gaaggagcgg ggaactgttc 1440  
gtggcattga ggacaacccc atggtggtgc cactttgcaa ccggtcgaag gacgtggtag 1500  
agcctctgct gcggygcgat gggtagcttc gctgcgggga gatggcccag gctgccagcg 1560  
ccgctgtgna ctcggggtga cctccgcac ctgcctgagg cccatcagcg cacatggyat 1620  
gcctggatgg acaacatccg ggagtgggtg atttccaggc agctktggtg gggccatsgc 1680  
atccagcct actttgtmac tgtmagtacc cagcgggtgc cctggggag gacctgaat 1740  
gggcggtact ggggtgagtgg acgcaatgag gcggaggccc gggagaaggc agccaaggag 1800  
ttcggagtgt cccctggaca agatcagctt ccagcaagat gaggatgtat tggatacctg 1860  
gttctcctct ggcctcttcc ccttatccat tttgggtgg ccaaccagtc agaagacctg 1920  
agtgtgttct accccgggac actgctggag accggtcatg acatcctctt cttctgggtg 1980  
gcccggatgg tcatgctggg cctgaagctc acgggcaggc tgccytttag agaggtctac 2040  
ctccatgcca tcgtgcgaga tgctcacggc cggaagatga gcaagtctct aggcaatgtc 2100  
atcgatcccc tggacgtcat ctatggaatc tccctgcagg gcctccacaa ccagctgtg 2160  
aacagcaacc tggatcccag cgaggtggag aaggccaaag aagggcagaa agctgacttc 2220  
ccagcgggga ttctgaatg tggcaccgat gctctccggt ttggattatg tgcctacatg 2280  
tcccagggtc gtgacatcaa cctgatgtg aaccggatac tgggttaccg ccacttctgc 2340  
aacaagctct ggaatgccac caagtttgcc ctctgtggc ttgggaaggg ttttgtgcc 2400  
tcacccacct cccagcccgg aggccatgag agcctggtgg accgctggat ccgcagccgc 2460  
ctgacagagg ctgtgaggct cagcaatcaa ggcttccagg cctacgactt cccggccgctc 2520  
accactgccc agtacagctt ctggctctat gagctctgtg atgtctactt ggagtgcctg 2580  
aaacctgtac tgaatgggtg ggaccagggt gcagctgagt gtgcccgcca gacctgtac 2640  
acttgccctg acgttggcct gcggctgctc tacccttca tgcccttcgt gacggaggag 2700  
ctgttccaga ggctgccccg gaggatgccg caagctcccc ctagecctctg tgttaccccc 2760  
taccgggagc cctcagagt ctctggaag gaccccgagg cagaagccgc ccttgagctg 2820  
gcgctaagca tcacgcgagc cgtgcgctcc ctgcgggccc actacaacct caccgggac 2880  
cgccctgact gtttctgga agtgccggat gaggccacgg gcgcccctggc atcgccgggtg 2940  
tcgggctacg tgcaggccct ggccagcgca ggtgtggtgg ctgttctggc cctgggggct 3000  
cccgccccc agggttgcgc tgtggtctg gcttctgatc gctgctccat ccacctgcag 3060  
cttcaggggc tgggtgaccc tgcacgggag ctgggcaagc tgcaagccaa gcgagttgag 3120  
gcccagcggc aggccagcg tctgcgggaa cgccgtgct cctcgggcta tcctgtcaag 3180  
gtgcccgtcg aagtccagga ggcagatgaa gccaaagctc aacagacaga agcagagctc 3240  
aggaaggtg atgagccat cgccctattc cagaagatgc tgtgatccac caccagctt 3300  
caccctcac cccagcggc tcacatggg gatggcagca ataaaatatt ttcccacaaa 3360  
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 3405

&lt;210&gt; 142

&lt;211&gt; 2268

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2169)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2196)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2232)

<223> n equals a,t,g, or c

<400> 142

```
gcctgcctcg agaggtgtgg ctccctggaga cccacagggc cgatgacttc tgggtgcgagg 60
gagaacccta tccaggtccc aagggtcttcc cttgaagcca ctggcgccca ggagcgggtg 120
gccgaagacg tgccctaccc taccacaagg gctgtgtctc taccocctag cctgggctgt 180
ggatctactg gaatgagcag cagccgcttc ctcggcagcc ttgggaagca cgggagactg 240
gacagcagcc gccgggcacg gttatggggg cgggggtggc ggggaggcta gattgtttcc 300
tggtactgtc actgccactg gggctttgat ttggaggaaat ggggcagggg actatctgaa 360
gcgcttccat cctaaagcca taatgaaaat atcttctctc cttccccatt ctatacaaaa 420
tactaagtgg tttctgtgct ccactccct accccttagt taaatagggt ttattttcca 480
ctcatgccct tatgcctttt tttcttatag ttttttaact tattgactgt gcatgaccca 540
gtggtttgaa ttgtttttag ttcaagtcac tggtaaaaac taggtttaag gagatgagct 600
actgtttaaa gtgagctggc ctgcctaatt aattccttgt gaaaactaaa tgattttttc 660
agtttgggga tcattctcac aacataacta tgcattgata ggacaagatt tattttcttt 720
cctccctttg ccagtaggcc acatctggtt tactcaggca gcatctacta agaaattcag 780
cacctgcata tctctgtgac atggtcactt agagcttata ttccctatga atctccagat 840
ctgtgagtcg agcagatttc atgttgacga ttcaccttta atgcaaagac tgtattatcc 900
tcacatgact ttttttcttg tottactgta ccttaaaagg tgatagagta attctgtatt 960
ttctaacggg aagattcaaa ggagctgaat gtgttatgct tccaaacaac tgaatgtaaa 1020
acactcctag ccagttgttg cattccctat atttatttac ttccaatatt ttactgtaaa 1080
agtagggaga aatattatgt tgatagttgt ttcatattct ctcagggaact ttaatgttcc 1140
cgactcgggt gattccagct gtgttgctgg cagtgtgtgc tcaacctctc cctaaaaatg 1200
actgagccct gggttcatct aatgtggttt tccttaggaa gagatagaag gcacagaaga 1260
tcacagctag agaattgaga attaactata ctactagcca ttttagggca ccaaaacttg 1320
ggattaaaca ctccctactt ccactccca actcctgaaa tgaagtcttg ctatctgtga 1380
ctagttttat ttttgtgctt ttaatagtcg gagcagtcct accttgttta cacatgtatt 1440
gacaccattt gcttcaggcc atggagcact gtttctccct ttttactatt tataggattc 1500
cgttttttca caagactttt aataaaaaa aattgtagaa ataaacacat taaaatttgc 1560
ccagctgtcg tctaagccct cttgattgac ttgcccaagt ggcaatagag ttctaataatc 1620
tataataaaa ggagatttgc tattattagt ggaatgttga ccccgatatg agagaaacag 1680
tacgtgcctt tscctcttta tgcacacaga gaccaggggt gagggagtat ttgttcccag 1740
tttttaagat agtataaaaa agcaaatact tggtagtgta tttaaaaaa aaaccaaacc 1800
aaaaacaaaa aagatattcc acaggacatg ccactttatt ataaaacctg acacaggcat 1860
agtaccaagt atttctgca ttgttgctaa aattgtttta ttgtagctcc acattctggt 1920
```

```

gtagttaaaa atgccttttg gggcagtttg aagcagttct tcatgccact tagtttgaaa 1980
ataaaattct agrtatgcaa atgattttct tagaaaactt cacaaaaataa aagatccttg 2040
tttttttcca tagcacagta atgaatgttg ttatcaatca catacttttt tggattatat 2100
tgtagcaaaa agttgattag cttaccaaga ttattaatag caatgtatgt gttataatac 2160
aacttagtna cattaagacc tacgaaaact catcnggct gtaggatagt aataaaggaa 2220
gaattatgac tncattatga aaaaaagaag ttttaaagtt ttcaatac 2268

```

&lt;210&gt; 143

&lt;211&gt; 1757

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 143

```

aattcggcac gagagcagca tcttatcagt tttgtttatt cgatttctaa aatgtgctga 60
tccttttaaa actcctgctt atctctgcaa caaagaaaaa tattcaaaaa tactgccttc 120
attttcacac acagtgtgta agatgctgca agaccaaata atagctcata aaatcaggtc 180
ctgagatagt taccataaaa gaggaatcct ttgagtgtat gccattgggtg agccgatgag 240
catggaccat agaagggctc aatgtagaag gtaaaattgg caaatcataa ttgagaaata 300
tgaaatgtat tcccatatat aatatgggtat aggggtgtaat gtacctgctt ttgatcactt 360
ttcattttta agtgctattc acttgatcctt aaatgttcca tgaactgtta aatttcttaa 420
gttacatagt tactacacca catttatgtg tatgttatgt tttaatatgc aatgataggt 480
atgtacaatt gataatataa aggggctcat tgaaacttga gagcctgttg agttttgggt 540
agttgtagat tgcattttta taaaaaaaaa tacagataga ttgatgataa tagatattgg 600
ggcattgttt ctgtctcatg agaattcttt tattcattac cataagcctt cactgatact 660
ataagcatta ttttaaatga cgctgatcctt aagcttgaaa taaatggaaa gcagaaaagg 720
tgagccagtt gatttgaatg cattggatat tagtgttaga aacaatgtat agtttagatt 780
gaaactgaac tgacttattt agcacttaaa caaaaatttg acaatgtttt tagttttttt 840
taagacagct tagtggtgtg atacttagaa ttctatgggt tgatgtttct tttagaaatg 900
agaagtatag ttttattttt taatataaaa aatgggtttt atactaaaac tagtaatttg 960
atactagttg tttataaaca ttgtaaaata tatcttttaa acaaatatc ttggtagtta 1020
attcataagg gtgggttttg gtaggaatag cagagtactt tcagagggaa aggggagtca 1080
ttcagaagtg atagcatttt atttgtttga atactctgcc agtaaaatca gctgtactta 1140
gaaagtatat tggtgtgtag aataatgatg tagagtttac taatcagtga ggatgtcttg 1200
tttttatttt ctgcaaaact tgcctcactt taaaatgcat tataacaata cctaattaaa 1260
gataaatttg gctctgaaag ttaccttatt tttgttgtag ttagtgactt catttttctt 1320
gccacaatat aagctttttg gggatttttt taaattgggt cttttaataa gcaataaat 1380
cccagggttt tattttcttc agtgataccc ctatagaaac tcttaaatgt atttgcgcat 1440
atatatatat atattttctt atgcatgctc gatgcatttt cgctctgaga aaaaatgttct 1500
ctacagaaac taccgtgtg taaaaagaag attggcttaa aatggctact gtgatgggaa 1560
cagtgtctta gggagatgca gcttggactt gaggtaaatt gaatacttta caactgtgg 1620
ttagagtttg ctttaatgac attgtatgta aaaggtcaca tgattgctgt aattttgtat 1680
tcattatggt ttcctcaata aatgtacatt gatgactatt aaaaaaaaaa aaaaaaaaaa 1740
aaaaaaaaaa aaaaatt 1757

```

&lt;210&gt; 144

&lt;211&gt; 1062

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (52)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1056)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 144

```
acccacgcgt ccgcccacgc gtccgcctgg actgtgaccc agccagcacc gnetctccta 60
gtggcaactg gctgggaatg gctgaggggc tacctactgc ttgcggcctg ccagcgggag 120
gaggggggag gaaagaagaa agggggcggg gttgaggggg gcgggcctgg acctggggag 180
tgaaagcgaa agcccgggcg actagccggg agaccagaga tctagcgact gaagcagcat 240
ggccaagccg tgtgggggtgc gcctgagcgg ggaagcccg aaacagggtg aggtcttcag 300
rcagaatctt ttccaggagg ctgaggaatt cctctacaga ttcttgccac agaaaatcat 360
atacctgaat cagctcttgc aagaggactc cctcaatgtg gctgacttga cttccctccg 420
ggccccactg gacatcccca tcccagaccc tccaccaag gatgatgaga tggaaacaga 480
taagcaggag aagaaagaag tccctaagtg tggatttctc cctgggaatg agaaagtcct 540
gtccctgctt gccctgggta agccagaagt ctggactctc aaagagaaat gcattctggt 600
gattacatgg atccaacacc tgatcccaa gattgaagat ggaaatgatt ttggggtagc 660
aatccaggag aaggtgctgg agagggtgaa tgccgtcaag accaaagtgg aagctttcca 720
gacaaccatt tccaagtact tctcagaacg tggggatgct gtggccaagg cctccaagga 780
gactcatgta atggattacc gggccttggg gcatgagcga gatgaggcag cctatgggga 840
gctcagggcc atggtgctgg acctgagggc cttctatgct gagctttatc atatcatcag 900
cagcaacctg gagaaaattg tcaacccaaa ggggtgaagaa aagccatcta tgtactgaac 960
cggggactag aagggaaaata aatgatctat atgttggtgt gaaaaaaaaa aaaaaaaaaa 1020
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaanaaa aa 1062
```

&lt;210&gt; 145

&lt;211&gt; 1030

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 145

```
aaactgactg ggggtcaattc aagtcattgca ggctgtgaga aacgcgggggt cgcggttcct 60
gcggtcctgg acttggtccc agacagccgg cagggtcgtg gccagaacgc cggccgggac 120
catctgcaca ggcgctcgac agctccaaga cgctgcggcc aagcagaaag ttgaacagaa 180
cgcggtccc agccacacca agttcagcat ttaccctccc attccaggag aggagagctc 240
tctgaggtgg gcaggaaaga aatttgagga gatcccaatt gcacacatta aagcatccca 300
caacaacaca cagatccagg tagtctctgc tagtaatgag ccccttgccct ttgcttcctg 360
tgccacagag ggatttcgga atgccaagaa gggcacaggc atcgagcac agacagcagg 420
catagccgca gcggcgagag ytaaacaaaa ggcgtgatc cacatccgag ttgtggtgaa 480
aggcctgggg ccaggacgct tgtctgccat gcacggactg atcatgggag gcctggaaat 540
gatctcaatc acagacaaca cccaatccc acacaacggc tgccgccccca ggaaggctcg 600
gaagctgtga tgggaaggag gcctgcactt ggacctgacc tcaagcctca gctccagtgg 660
gaccttgtaa aatgtccctt gtcagagctc tccagaatat gcttggtgga gatccttcag 720
gcagtaaggg agagttttgc ctcttacac agtggccttt gcttgacact ccagctggag 780
atgggtgtgc cccaaagta agctttgcat ctcttacaag aggggagcta caggggcagc 840
cgtgcctagg cccaaactct gctctgagaa aataaatatc tgtaccacct gtcataattt 900
tgagattttt tgctttcaga gttacgtaat tcctaattcc tcttgaaaaa gagagtgtga 960
aatgaggtga ggcctcagat gaaagtaaaa tataaatgtg agttgctatt taccagaaaa 1020
```

aaaaaaaa

1030

&lt;210&gt; 146

&lt;211&gt; 814

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 146

```
ggcacaggcc aggtcgtgcc agcatccgcc ggacgccgga agtgggttctc cgccccctgcc 60
actgggcat ggagactgtg gcacagtaga ctgtagtgtg aggtctcgcg gggcagtggc 120
catggaggcc gtgctgaacg agctggtgtc tgtggaggac ctgctgaagt ttgaaaagaa 180
atttcagtct gagaaggcag caggctcggg gtccaagagc acgcagtttg agtacgcctg 240
gtgcctggtg cggacaagta caatgatgac atccgtaaag gcatcgtgct gctcgaggag 300
ctgctgccc aagggagcaa ggaggaaacag cgggattacg tcttctacct ggccgtgggg 360
aactaccggc tcaaggaata cgagaaggcc ttaaagtacg tccgcgggtt gctgcagaca 420
gagccccaga acaaccaggc caaggaactg gagcggtcga ttgacaaggc catgaagaaa 480
gatggactcg tgggcatggc catcgtggga ggcatggccc tgggtgtggc gggactggcc 540
ggactcatcg gacttgctgt gtccaagtcc aaatcctgaa ggagacgcgg gagcccacgg 600
agaaacgctc aggagggcct gtccatcctc gctgtccttt cctgttctc cccctgcccc 660
ccgtctctat cctctgtggc cttcagctaa tttctgtctc cctgagattc gtccttcagc 720
cccatcatgt gctttgggat gagtgtaaat aaaacggggc tgtggccttg gaaaaaaaaa 780
aaaaaaaaa aaaaaaaaaa aaaaaagggg gggg 814
```

&lt;210&gt; 147

&lt;211&gt; 2678

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 147

```
cccacgcgtc cggatgaaca cgatgagaat aatgctgaag ctagtgtga attatcaaat 60
gaaggggtaa tgaaccatag aagcgaggaa gaacgtgtaa ccgaaacaca gaaaaatgag 120
cgtgttaaga agcaacttca ggcattaagt tcagaattag cccaagccag agatgaaacc 180
aagaaaacac aaaatgatgt tcttcatgct gagaatgtta aagcaggccg tgataagtac 240
aagactctgc gacagattcg acaaggcaat acaaagcagc gtatcgatga gtttgaagca 300
atgtgagagc tgttattttg catatatgtt cttcataagc tgaaccacca acagagaaaa 360
gcaggccttt gcagatatga tggaatgcat cccaccttgc caaagcactt acaccagttt 420
gactgtgcta gctaaaagac aaatttaagg ggagctcttc aacattaagg cagtatgata 480
tcatgcttgg ttttctttt tcttttggc cagggaatgg agaattggtg tccattgcct 540
cttttcacat ttttttctt tttcttttt ttttctgttg aagattaaca ctaattatca 600
cgtctgacaa atgtgtatgt gtggtttcag ttctgtgtac attttaaagg ataattgta 660
acattttaat gggtttccct tgccctttcc atatttaacc tatttccaca ttctctctca 720
ctcacatttt ctcaagtgtc ccttctctta tctgccatgt ccatagccat aattccacca 780
tcatacagat caggcagtgt ttaaaatgat ggtaggtagc acagtggaca gtctttgatc 840
atcatgtaga atatggctat gaatcaggaa agagattaga acatttaata atgtatgtac 900
agctggtgct tagttttttt ttaatctaaa ttaattacc ttattggata tttgatattt 960
ggttatttaa tcacagtcac ctttaacagc ttacactgat tgggttttta tctcctgtga 1020
tcctttgatg gctttttttg cctaccattt cacagagggt tagacagcag tagtagctcc 1080
ctaggagagt ttactgatga aacagcctct gcaagatttt aaaagttttg ttcttttata 1140
gactgattta gaaaaacaaa tgattagtta aaaaaagaaa atatacattt gttggttaact 1200
aatgttattt tttaaaacct ggacctttcc tggragggca gcatataara acatcagtgc 1260
ccgaggaggg gacaacaata ctacctact actacatctg tgatgactgg ttgttcaaac 1320
```

```

acaatggagt gtgtaaggta tatgttttat aattcataac catagcctcg atcatcaaga 1380
aatactttcg aaatttcatt ttccttcaga atatcttaag agtgctaaat ttttaactgc 1440
ctttttgtcg agtcaaactg tgggattctg atttgtatta aaattgtaag ctccctcactg 1500
gtatactatc atcctggagg ggtgtgtgat ggctgagcaa gagagagaga gaatgagaga 1560
gagactgtgt gtgtgtgtgt gtgtgtgtgt actctgtgtg tgtatgagag agagaaatgc 1620
taaccttgta gcatgtgaag aatgtctgta ccttgatacg atagttacat aatcagtata 1680
tttggtttct agatcactgt gcttattttg tttcaatctc tgactaaaaa tacttaaatt 1740
tggtttgta attccttatt tagaaattat aatttttagt tatattaatt tcggttatag 1800
cttactgaag aaatctttcc agttagaagg aggttctaatt attcacatgt tctaatactt 1860
tgtttattgt aaaacagcta aatttggaag tacgtaaagc cttgttttct ctgtgtgggt 1920
cagctacttt ccatttggtg ttacacagtc aaatttacat ttatctatta aaattgccat 1980
tttattaaac attttcatgc acagtagatt caagttgtgt ctgaaaatat ctcttgtgct 2040
tttttgattt tgctgacttt aaaaggatta atctgggcag acattatgta aaagaaaggt 2100
tgcgtttaat atattttttg aactttgtag gacaaaacat agctgggtaa ccttgaaagt 2160
actgttgtac catggtgtgt cacatgcttc agaatcctat ggaagagaat attcctactt 2220
gcagtacatc aaaggaaatgg atggtggacc ctactattca tgttttgaga cataaatgtt 2280
cactttaaag caattgcata atagataaaa acctgaactt tcattggatt tttgttaatt 2340
ttcctcattt tgaattatgt gcactacat agctacatca gtttgataca gtattgaaaa 2400
attatcagtt atattttgcy gtttatgrtc tattttagr ttaggrrtaa aatggrttta 2460
atccattttt aaggstgtgt gaatttttct aaacaagaac catttgcaat atggatttct 2520
tagagattaa accaattata acttattagc agtsgcgagc acatgttcat atagtcaatg 2580
taaaaatata ctaatgagta tttggtaaat cccagtaggc ttttaccatt agcataattt 2640
tgtgtgttac ctcggccgcg accacgctaa gccgaatt 2678

```

&lt;210&gt; 148

&lt;211&gt; 1028

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 148

```

ctgcctcagc ctcccagagta gctgggatta caggcacaca ccaccacgcc cggctaattt 60
tttgtgtctt tttagtagag acgggggttc gctatgttgg ccagactggt cttgaactgc 120
tgacctcgtg atccgccgcg ctcggcctct caaagtgtg ggattctgtg tgttttgtgc 180
acctccactt taggtaatca tagggagcac atttacagga tggctctaata acatgaaaac 240
aggctagttt caagcaacag caatgtcggg tggaagcag gcgtcatttg cttgaaaaa 300
agccttttga caacatacag gcattctttt aaaaccaggc tgaaacattt tatttccgag 360
acttaacggt gtgtttcctg tttcttaaac ctagcacctc tgtgtatttg aaaataatga 420
gacatctttc attggatttt ggaaaattgt tccccatggg attctaacct cactaccaa 480
tgagtgaag cttgattaag agttcttcca tatactagcc tccttggaag aagtgatcag 540
aagggtataa gaaggacaga aaggactatt ttaaagtgg actgaaggag aaaaaagcaa 600
aattcttggt tcatcccaat tctagttaga acaaagttaa acccccgtaa tcttaaagag 660
aaaatctttg gaggttttaa ttaaactttt tatacattta aagtcttggt aatggtgctt 720
taagtgtcaa ttagcatgtt aaaaggcttt gtacagacag gtaaaagttc catttctgag 780
tgatgaaatg taacacttct tcatctttta cttgaaatca aaactatcag attttatttt 840
tgtataatth aaggaaggta aagttagggg actagaagac tctaaattgg cttctacaga 900
tcaataatth aaatgtaact agttgggatt ttatagttaa aattatattt gtgtatataa 960
cataactaat ctgtaaattg taataaatat atttgcaatt attaaatgtt aagtgatatt 1020
ttggttca 1028

```

&lt;210&gt; 149

&lt;211&gt; 1425

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (647)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1359)

<223> n equals a,t,g, or c

<400> 149

```
gcgtctccgg aagtggaggc gggagcggca cggcagccac tgcttggggt agcgggaggg 60
cagactctgg ggcgcaactcc cgggccggtc atgaacgggc cggcggacgg cgaagtggac 120
tacaaaaaaaa aataccggaa tctgaagcgg aagctcaagt tcctcatcta cgagcacgag 180
tgcttccagg aggagctgag gaaagcggaa aggaaattac tgaaggtgtc ccgggacaag 240
agtttccctcc tagaccgact tctgcagtac gagaacgtgg atgaagactc ttcggactca 300
gatgccactg catcatcaga taacagcgag acggagggga caccacaagt gtctgacaca 360
ccggcccccta agaggaagag aagccctccg ctggggggcg cccctctccc ctccagcctc 420
tccctgcctc cttcaacagg gtttccccct caggcctccg gggtccccct ccataacctg 480
agctcgctgg cctcctcccg ctacccccca ttcccttctg actacctggc cctgcagctg 540
cccgasccca gtcccttrag gcccgaagcg gagaaacggc cccgmctgcc ccggaactc 600
aagatggcgg tgggaccccc cgaytgccct gtgggagggc cgctganctt ccctggccgg 660
ggtytgggg stggggtcgg gamaaccctg amccccctc caccacctaa gatgcccccc 720
cccacgatcc tgagcacggt ccctcggcag atgttcagcg atgcaggtag cggggacgat 780
gccttggtat gagacgatga cctggtgatc gacatcccgg agtgaccgtg acatcacgcc 840
atgcccacca cggccccgcc cggcgccctc cccgtgccag cacacacgag tccagcttcc 900
tcggaggtgt ttattgatgc ccagctgccg tgctccggcc actgacacaa ccagaaaagg 960
cgtaaacaatg cacgggtgtc cccagaggag gtgcaggggc cctgccttca aaccccgggc 1020
ccctccaggg gacagttatt taaacgagtg gccgggagca tctgccacct gctggggagg 1080
cagagaccct gcaatggcca cctctttaa agggcagctg tacagggeta ggttttttca 1140
atgaagtttc tgtattaaag gagtggctct gggtttgttt tttgtccttt ttttttgaga 1200
cattctcctc ctctgaacct cccctaattc gacctcctcc ctgttggggg agagggacgg 1260
ggcagcgtgg agaggcacga gtgaggagcg cgggggcctg gggccgggct ctgagcactg 1320
cccggtgtg cagatgatgg ggggtttgca tatttgcan ggactagcga gtcaggcagg 1380
aggtttgcat atgtgaatat agaactccgc agccctcat gagca 1425
```

<210> 150

<211> 780

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (285)

<223> n equals a,t,g, or c

<400> 150

```
gctgcgagaa gacgacagaa ggggagagcc aatggaaagg ggctgccgcg cggccgtaaa 60
```

```

gagttttag agcagttcgg gtgcggtacg ttgcattccg gtaccggacg ccgagagcgg 120
tttgtctccg tctctggagt ttagggcag aggtgatcat gtccggtcgc gggaaacagg 180
gcggcaaaagt gcgagcaaag gccaaatccc gctcctcccg cgcgggcctg cagttcccgg 240
tgggccgagt gcacagactg ctgcgcaaag ggaactacgc ggasnagtgg gcgccggggc 300
gccggtgtac ctggcggcgg tgttgagta ccttacggcg gagatcctgg agctggctgg 360
caacgcccg cgtgacaaca agaagaccag gataattccc cgccacctgc agctcgccat 420
ccgcaacgac gaggagttaa acaagctgct gggcaaagt accatcgctc agggcggcgt 480
cctgcccac atccaggccg tgctgctgcc caagaagacg gagagtcaga agacgaagag 540
caaatgaccc tgacgccgcc ctccaggagc tggtccsc agcaaaggcc cttttcatgg 600
tcgtcccga atgcttttga atgtgctgga tgcattggag ggccggtgac atctagcggg 660
gaggtggcg gcgagggtcc cggcgggagc caataaaagt ggtgaaaatc gtaaaaaaaa 720
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780

```

<210> 151

<211> 1066

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1061)

<223> n equals a,t,g, or c

<400> 151

```

ggacccgcc tggcgcgga gaaggtgcgt ccgcggtga tcgaggagct ggcccgcgc 60
gtgcgcgcc tgcgggagca actgaacagg ccgcgcgact ccagctcta cgcggtggac 120
tacgagacct tgacgcggcc gttctctgga cgccggtgc cgtccgggc ctgggcccac 180
gtgcgcgcg agagccgcct cttgcagctg ctccggccgc tcccgtctt cgccctgggc 240
cgctgtgta cgcgcaagtc ctggtgtggt cagcacgacg agccgtgcta ctggcgccctc 300
acgcgggtgc gcccgcacta cagggcgag aacttgacc acgggaaggc ctggggcatc 360
ctgaccttca aagacgcctc tttttcttca tcagggaaga ctgagagcga aggcgcggga 420
gatcgaacac gtcattgtacc atgactggcg gctggtgccc aagcacgagg aggagccctt 480
caccgcgttc acgcgggcgc cggaagacag cctggcctcc gtgccgtacc cgctctcct 540
ccgggccatg attatcgag aacgacagaa aaatggagac acaagcaccg aggagcccat 600
gctgaatgtg cagaggatac gcatggaacc ctgggattac cctgcaaac aggaagacaa 660
aggaagggcc aaggcacc ccgtctagaa tgccagaacc agcgggtggc cttaggggct 720
gtgaggcagt ggggacctta ttgatgaaag aaaccgtctt tgcgttacac ccgagtctgc 780
ctctcggagc agggagctca ccttcgcga cgtgttctga ggtctgcat cttagggggg 840
agggctgggg caaatcgcca cctgtgcctt tcctctggcc ctgctgcccc cacaccaac 900
tccgagggcc cagctgggg aaagcgggaa gcgctcgctc ctttcccc attagtgtc 960
tctctgcctg gatcccgga gaagctatga aagggaataa agagaaaaga artamaaaaa 1020
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa nccctt 1066

```

<210> 152

<211> 1649

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1543)



<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1579)

<223> n equals a,t,g, or c

<400> 152

```
accccggtc tccaaggagg tgtgacatca tcatcatctc tggccggaaa gaaaagtgtg 60
aggctgccaa ggaagctctg gaggcattgg ttcctgtcac cattgaagta gaggtgccct 120
ttgaccttca ccgttacgtt attgggcaga aaggaagtgg gatccgcaag atgatggatg 180
agtttgaggt gaacatacat gtcccgccac ctgagctgca gtctgacatc atcgccatca 240
cgggcctcgc tgcaaatattg gaccgggcca aggctggact gctggagcgt gtgaaggagc 300
tacaggccga gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc 360
ccaaatacca tccaagatt atcgggagaa agggggcagt aattaccaa atccggttgg 420
agcatgacgt gaacatccag tttctgata aggacgatgg gaaccagccc caggaccaa 480
ttaccatcac agggtagcaa aagaacacag aagctgccag ggatgctata ctgagaattg 540
tgggtgaact tgagcagatg gtttctgagg acgtcccgtt ggaccaccgc gttcacgccc 600
gcatcattgg tgcccgcggc aaagccattc gcaaaatcat ggacgaattc aaggtggaca 660
ttcgcttccc acagagcggg gcccagacc ccaactgcgt cactgtgacg gggctcccag 720
agaatgtgga ggaagccatc gaccacatcc tcaatctgga ggaggaatac ctgctgacg 780
tggtggacag tgaggcgctg caggtataca tgaaccccc agcacacgaa gaggccaagg 840
caccttccag aggctttgtg gtgcgggacg caccctggac cgccagcagc agtgagaagg 900
ctcctgacat gagcagctct gaggaatttc ccagcttttg ggctcagggt gctcccaaga 960
ccctcccttg gggcccaaaa cgataatgat caaaaagaac agaaccctct ccagcctgct 1020
gacccaaacc caaccacaca atggtttgtc tcaatctgae ccagcggctg gaccctccgt 1080
aaattgttga cgctcttccc ccttcccag gtccgcagg agcctagcgc ctggctgtgt 1140
gtgcggccgc tcctccaggc ctggccgtgc ccgctcagga cctgctccac tgtttaacac 1200
taaaccaagg tcatgagcat tcgtgctaag ataacagact ccagctcctg gtccaccg 1260
catgtcagtc agcactctgg ccttcatcac gagagctccg cagccgtggc taggattcca 1320
cttctgtgt catgacctca ggaataaaac gtccttgact ttataaaagc caaacgtttg 1380
ccctcttctt tccccacct cctcctgcca gtttcccttg gtccagacag tcctgtttgt 1440
ggagtgaat cagctcctc cagctgccag agcgctcag cacaggtgtc aggtgcaag 1500
gaagacctg caatggacag caggaggcag gttcctggag ctnggggggt acctgagagg 1560
cagaggggga cgggttctna ggcagtctg attttacctg ccgtgggggt tgaaarcacc 1620
aagggtccct gacctacct cactgcca 1649
```

<210> 153

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (35)

<223> n equals a,t,g, or c

<400> 153

```
ccggaaattc ccgggtcgac ccacgcgkcc gcggnagwgc tcacacgtgt gtcacctgcc 60
ctgctcctgg ccccttgccc ggccgggctg tttctggcca tgggtcgctc ccgccggaca 120
ggcgcgcacc gagcgcactc tctagcccgg cagatgaagg cgaacggcgg cggccggact 180
```

tggatgagat tcaccgcgag ctgcggcctc agggatccgc acgacccag cccgacccaa 240  
acgccgagtt cgaccccgac ctgccagggg gcggtctgca ccgctgtctg gcctgcgcga 300  
ggtacttcat cgattccacc aacctgaaga cccacttccg atccaaagac cacaagaaaa 360  
ggctgaagca gctgagcgtc gagccctaca gtcaggaaga ggcggagagg gcagcgggta 420  
tgggatccta tgtgcccccc aggcggctgg cagtgccac ggaagtgtcc actgaggtcc 480  
ctgagatgga tacctctacc tgacatggcc tgaagatgca ggcagagga attgcccattg 540  
gacagtgacg caaggactag gctgggaggg agcgtgccaa ccccttttgc ctctgggttt 600  
ggggagcggg ggcctcttc ttggtgccct gcccacaata aaggaactgg acaaagagaa 660

<210> 154

<211> 605

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (449)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (574)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (578)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (583)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (587)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (596)

<223> n equals a,t,g, or c

<400> 154

ggcagagctc caccttccat ccggcgccgg ctttcggcgc gacggtcgcc gcgttccatc 60  
gtcgcgcggc ccttcgggcy cccgagcccg caatgtcggg cccaacgga gacctgggga 120  
tgccgggtgga ggcgggagcg gaaggcgagg aggacggctt cggggaagca gaatacgtg 180  
ccatcaactc catgctggac cagatcaact cctgtctgga ccacctggag gagaagaatg 240  
accacctcca cgccgcctc caggagctgc tggagtccaa ccggcagaca cgctggaggt 300  
tccagcagca gctcggggag gccccagtg atgccagccc ctaggctcca agagcccca 360

```

accgggaccc aaccctgcct ccctgggcta ggctctggcc tgggcactca mcccctggct 420
tagacamctt ctcaagggtt ggccttcang gacccctggt gggctctgcct gcctgggcca 480
accttcctgc ctgggscctc ccttggctam ctgggscagc cccacccaac tggcatgccc 540
tcctgggggc caaagaatgg ggcctgcaac ccancantt gcntgcncaa cccaanttcc 600
tggggg                                           605

```

<210> 155

<211> 695

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (173)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (499)

<223> n equals a,t,g, or c

<400> 155

```

gaaccctaga aaaaaggatg cagtactaaa gtgtcattca ttcaaagcca ctctcttttt 60
gggtattccac ccattttcca gacggtgaca ctgaggctca ggaagcagta gggacttgca 120
caaagccctt tgggaagcag gctgggaaac agtggaggga ggggtgtccat tanccccaag 180
gagacacagg atctgggctc tktytttsgc cttcctccca gaatacgtg ccatcaactc 240
catgctggac cagatcaact cctgtytgga ccacctggag gagaagaatg accacctcca 300
cgcccgccct caggagctgc tggagtccaa ccggcagaca cgcctggagt tccagcagca 360
gctcggggag gccccagtg atgccagccc ctaggctcca agagccccc accgggaccc 420
aaccctgcct ccctgggcta ggctctggcc tgggcactca cccctgggt tagacacctt 480
ctcaagggtt ggccttcang gacccctggt gggctctgcct gcytgggcca cccttcctgc 540
ctgggrcctc cccttgkkc tactggggcc agccccacc acctggcatg ccctcctggg 600
gccaagagtg ggcctgcaam ccacccattg setgcccac caattcctgg gcgytcccca 660
wtytgcaccag gcttgaatgt tcacatgaaa tgggt                                           695

```

<210> 156

<211> 780

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (289)

<223> n equals a,t,g, or c

<400> 156

```

cggtgggctc gcgttgagge tgcggtcag gagggagcag gagctggatc cggcttccgg 60
aaggagctgg tgagcaggct gctgcacctg cacttcaagg atgacaagac caaagtgagc 120
ggggacgcgc tgcagctcat ggtggagtgt ctgaaggctt tcgttggtga agcagcagtc 180
cgcggcgtgc ggcaggccca ggcagaagac gcgtccgtg tggacgtgga ccagctggag 240
aaggtgcttc gcagctgctc tggacttcta gggatctcag ccgtggckna ggccaccccc 300

```

```
agaggagccc ctggtccaca gaagcaggcc ttgtgtttcc agcggcctct gataagaggc 360
aggggaaggam ctgaaggatt tggarttgat tcaaacaaga tctctgggag tctccagcct 420
gtgcagaagg ggcaggactg cagtgcactg cgggccttgg agtgtccagt ggggacactg 480
gtgtgggaag gggcagcacc tggggagtcc ctgcctctcc tccctgggac aatagtgtgc 540
atgccacccg gggtcctaca ggcagggtgct gggaaggcc tggccagcag gtagcctgtg 600
tgtttgacaa acagcagctg gcagcgtgc ctctgccc cattcctgcc acccgacatc 660
aaagctggcg tgtgacctt ccagccatgc gatattcccc ttggaagatg cttccccagg 720
ctataaattt gttctcacia agcaacatca ataatcaaa actgtctcty ccaaaaaaaaa 780
```

<210> 157

<211> 1127

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1113)

<223> n equals a,t,g, or c

<400> 157

```
aacttcagt ccctcactgt agaatttaaa agccttactg ttgattgccc atggtggact 60
tgatggagaa attaaatata ttccattatg ctttacaaaa tactgtatat gtttcagcaa 120
gtttggggaa tgggagagga caaaaaaaaa ttacatttaa tctatgcatt ttgccaagc 180
catattgagt tattttacta ctagagacat taggaaacta actgtacaaa agaaccaagt 240
ttaaaagcat tttgtggggt acatcatttc tataattgta taatgtattt ctttgtggtt 300
ttaaatgata aagacattaa gttaacaaac atataagaaa tgtatgcaat gtttgaaatg 360
taaattatcc ttagaacact ttcaatgggg gttgcattgt ccttttagtg ccttaatttg 420
agataattat ttactgcca tgagtaagta tagaaatttc aaaaaatgta ttttcaaaaa 480
attatgtgtg tcagtgaagt ttccattgat aattggttta attttaaata ttttagaggtt 540
tgttggactt tcataaaatt agtacaatct ttgcatcaaa ctacctgcta caataatgac 600
tttataaaac tgcaaaaaat gtgaagggtt gcaccaacat aaaaaggaaa tatggcaata 660
catccatgat gttttccagt taacatagga attaccagat aaatactggt aaactcctgt 720
ccagtaacaa gagttgattc atatggacag tatgatttat tgtttatttt ttaacccaaa 780
tacctcctca gtaatttata atggccttgc agtaatgtgt atcagataag aagcactgga 840
aaaccgatcg tctctaggat gatatgcatg tttcaagtgg tattgaaagc cgcactgatg 900
gatatgtaat aataaacata tctgttatta atataactaat gactctgtgc tcatttaatg 960
agaaataaaa gtaatttatg gatgggtatc ttttaatttt actgcaatgt gttttctcat 1020
ggctgaaatg aatggaaaac atacttyaat tagtctctga ttgtatataa atgtttgtga 1080
aattccatgg ttagattaaa gtgtrttggg aanaattctc catggggg 1127
```

<210> 158

<211> 1282

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (120)

<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (205)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (207)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (236)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (732)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1279)  
<223> n equals a,t,g, or c

<400> 158  
tgctctacaa atagtaaaaa taaaaaataa aaaaagtagc tgggcgtggt ggtgtgcacc 60  
tgtgggtccca gctgcttggg atgctgaggt ggaaggatct cttaaaccce ggagggtggn 120  
aggctgcagt gaacttgcca ttgcaccact ggcactccag tctgggggac agagtgcagac 180  
cccatctcaa aaaagtgttt aattnantat acttgtagt ggtctatttg catttnaaaa 240  
ctgctttcta gaattaggat agctccctta ggtttaatgt tttggtgagc aggaatatca 300  
gttacccttc cagatcttaa ttctagtttt tttatcactt tttcatgagg tgatctcatc 360  
ctcatctcct agcatgtctg gcaattttga tttctgaact ctgtgctacc tcagaggcca 420  
gcttccttag ggaaaaatca gtgctgaaat aaagttatat ttccttttct gctctaaata 480  
tatagtgggg gaataagaga aatgaagagg aattcctgag aacgtaatta ctagaaactc 540  
ccctctccca cgtaattgtc ctcacacacc atggaccctt attccccca tttgcgacct 600  
cccacccac cccacaacag gtggtgatct ttgtgaagtc tgtgcagcgg tgcattgcct 660  
tggcccagct actagtggag cagaacttcc cagccattgc catccaccgt gggatgcccc 720  
aggaggagag gntttaaaga ttttcaacga cgaattcttg tggctaccaa cctatttggc 780  
cgaggcatgg acatcgagcg ggtgaacatt gcttttaatt atgacatgcc tgaggattct 840  
gacacctacc tgcctcgggt ggccagagca ggccggtttg gcaccaaggg cttggctatc 900  
acatttggtg ccgatgagaa tgatgccaa atcctcaatg atgtgcagga tcgctttgag 960  
gtcaatatta gtgagctgcc tgatgagata gacatctcct cctacattga acagacacgg 1020  
tagaagactc gccattttg gaatgtgacc gtctgtcctt caggagagga caccagggtg 1080  
gggggtgaagg agacactact gccccaccc ctgacagccc ccaccccatg gcttccatct 1140  
tttgcacac caccactcct gaaccccat ttctgatttg tcagaatttt tttttaacaa 1200  
aactaaaaat gaaacacatg tgtctgtggt atctaaaaaa aaaaaaaaaa aaawwggggg 1260  
ggsgcccgta cccattggnc ct 1282

<210> 159  
<211> 1505  
<212> DNA

<213> Homo sapiens

<400> 159

```
ttacatgttg cagaagctaa ttgaagagac agataggttt gtagtggtca cagaagagga 60
atcaggcatg agtgaccagt tgtgtggcat tgctgcctgc cagacggatg acatatacaa 120
ccgaaactgc cttattgaat tggccaacct gtcagatggt tcttcgtgga gcagagacak 180
aaggctgtgt catttgtgtca gctgccaaag cccaactgct gcagtgccag caccatccag 240
cctggtatgg tgatacattg aagcaaaaga catcctggac ttgcctcttg gatggcatgc 300
agtactttgc caccactgaa agcagcccca cagagcagga tggccgacag ctctgggttag 360
aggtgaagaa tatcgaggag caccggcagc gtagtctgga ctctgtgcag gagctgatgg 420
agagtgggca ggcagtgggc ggcatggtta ccacaaccac agattggaac cagccagctg 480
aggcacagca agcccagcaa gtccagcgga tcatttcgcg ttgcaactgc cgaatgtact 540
atattagtta cagccatgac attgatcctg aactagcaac tcagattaag ccacctgaag 600
ttcttgagaa ccaggaaaag gaagatctcc taaagaagca ggaaggggct gtggatacct 660
tcaccttat ccaccatgag ctggaaatth ccaccaaccc agctcagtat gccatgatcc 720
tggaattgt caacaacctg ctgctccatg tagaacctaa gcggaaggaa catagtgaga 780
agaagcaacg ggtcagggtc cagcttgaga tctctagcaa tccagaggag caacgcagca 840
gcatactgca tttgcaggag gctgtgcggc agcatgtggc ccaaatacga cagctggaga 900
agcagatgta ttctatcatg aagtctttgc aggatgacag caagaatgag aatctgcttg 960
acctgaacca gaagcttcag ttgcagctaa accaggagaa ggccaacctg cagctggaaa 1020
gtgaagaact gaatatcctc atcagggtgt ttaaggattt ccaactgcag cgggctaaca 1080
agatggagct gcgaaagcac aagaagatgt gagtgtggtc cgtcgcactg agttttactt 1140
tgctcaggca cgttgggcgc tgacagagga agatggacag ctgggaattg ctgaattaga 1200
actgcagagg ttctctaca gcaagggtgaa taagtctgat gacacagcag aacatcttct 1260
ggagtgtggc tggtttacca tgaacaacct cctcccaaat gctgtctata aggtagtact 1320
gcggccccag agtcctgcc agtctgggcg acagctagct ctccgcctct tcagcaaagt 1380
tcggccccct gttgggggta tctctgttaa ggagcatttt gaggtaaatg tgggtgctctc 1440
accatccagc tgacacacca ttcttcaca gatgatgggc ttttctttcc tggccgaagt 1500
gtgga 1505
```

<210> 160

<211> 736

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (718)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (723)

<223> n equals a,t,g, or c

<400> 160

```
aggcacgagg gacacttggg gtctggacgc aacggcggcg ggagcatgaa cggccctcca 60
gccttcgagt cgttcttgct cttcgagggc gagaagatca ccattaacaa ggacaccaag 120
gtacccaatg cctgtttatt caccatcaac aaagaagacc acacactggg aaacatcatt 180
aaatcacgtg cctgcttccc cttcgccctc tgccgtgatt gtcagtttcc tgaggcctcc 240
ccagccacgc ttctgtaca gcctgcagaa ctgtgagtca attaaacctc ttttcttcat 300
```

```

aaattaccca gtttctcata gttctttata gcagtgtgaa aacagactaa tggacccttc 360
tggttgaagg aatgcagcca ttctgcttgt ttgactatgt cctttctatt catctctatt 420
tcctgggagg tgtttatcca agtgcaatag gaggtattgg tgaccgcaca gtcccctcag 480
tgttctgcta gtaaatagtt gaaggttgat cattgatctt ctgcgttttc agtctggcat 540
ggaaaagccc ctgtgcaact ggtaaagata tcaataagca cctgggtgggt ggcgggggta 600
gtccaggctt gtcttgcaac tgtatgttct cttcagaccc ctccctggcg atgccagatt 660
cactgggctg gcagattctg ccccccccaa aaaaaaaaaa aaaatattaa taataaanaa 720
aanagactcc caggga 736

```

<210> 161

<211> 995

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (59)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (889)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (899)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (928)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (933)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (938)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (974)

<223> n equals a,t,g, or c

<400> 161

gggtcgaccc acgcgtccgg gcggcctcgg cagcgggtgtt ctcgcgcttg cgaasgggnc 60

```
tccggctcgg ctgcggggga ctgtgcacga ggttggcgac gcgccccgcc gggccccaga 120
tcaggccgca gagatcggga gccgcgggag cactaaggcg caagggccac agcagcagcc 180
gggctcagag ggtcccagct atgccaaaaa agttgcgctc tggcttgctg ggctgcttgg 240
agctggtggg actgtgagcg tcgtctatat ctttggaac aaccggtgg acgaaaatgg 300
tgccaagatt cctgatgagt tcgacaatga tccaattctg gtacagcagt tgcgccggac 360
atacaaatat ttcaaagatt atagacagat gatcatcgag cccaccagcc cttgccttct 420
cccagaccct ctgcaggaac cgtactacca gccaccctac acgctcgttt tggagctcac 480
cggcgctcctc ttgcatcctg agtggctcgt ggccactggc tggaggttta agaagcgccc 540
aggcatcgag accttgttcc agcagcttgc ccctttatat gaaattgtca tctttacgct 600
agagactggc atgactgcgt ttccactcat tgatagtgtg gaccccatg gcttcatctc 660
ctaccgccta ttccgggacg ccacaagata catggatgga caccatgtaa aggatatttc 720
atgtctgaat cgggacccag ctcgagtagt agttgtggac tgcaagaagg aagccttccg 780
cctgcagccc tataacggcg ttgccctgcg gccctgggac ggcaactctg atgaccgggt 840
cttggtggat ctgtctgcct tcctcaagac cattgcactg aatggtgtng gaggacgtng 900
cgaaccgtgc tgggagcatt atgccctngg ganggatnga ccccgctggg cggcttttgc 960
aaacagcggc aaancgggct tagaagcagg gagga 995
```

<210> 162

<211> 1125

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (972)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1023)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1077)

<223> n equals a,t,g, or c

<400> 162

```
gccctagtagt ggtccggaat tcccgggtcg acccacgcgt ccgcccacgc gtccgcgctg 60
gtgttgccggc gctggcgaca gtcgggggtg cgagcggccc ggggcccggg cggccagggc 120
cgctgcagga cgagaccctg ggtgtggcgt ccgtgccctc gcagtggagg gccgtccagg 180
gcatccgcgg ggagacgaaa agttgccaga cggccagcat tgccactgcc agtgcacccg 240
cccaggccag gaatcatgtg gacgcccagg tgacagcagga gggccccgtg cctgtcagcg 300
tgacgcccc gtcccagtay gacataccca ggctcgcagc ctttcttcgg agagtggagg 360
ccatggtcat ccgagagctg aacaagaatt ggcagagcca cgcgtttgat ggcttcgagg 420
tgaactggac cgagcagcag cagatggtgt cttgtctgta taccctgggc taccgccag 480
cccaagcgca gggctgcat gtgaccagca tctcctggaa ctccactggc tctgtggtg 540
cctgtgccta cggccggctg gaccatgggg actggagcac gcttaagtcc ttcgtgtgtg 600
cctggaacct ggaccggcga gacctgcgc cccagcaacc gtcggccgtg gtggaggtcc 660
ccagcgtgt cctgtgtctg gccttcacc ccacgcagcc ctccamgtc gcaggaggc 720
tgtacagtgg tgagggtgtg gtgtgggacc tgagccgtct tgaggaccg ctgctgtggc 780
```



```

gcacaggcct gacggatgac acccacacag accctgtgtc ccagggtggtg tggctgcccc 840
agcctgggca cagccamcgg ttypaggtgc tkagtgtggc cacygacggg aaggtgctac 900
tctggcargg catcggggta rgccagctgc agttcacaga rggcttcgcc tggttcatkc 960
agcagctgcc anggagcacc aagctcaaga agcatccccg cgggagaccg aggtggggcg 1020
canggcaggc tttcttccag tttgacctca ggttttcatt ttggcaggaa gcggttnccg 1080
ttcaattttc ctggcattgg agagcagcct taaggggtgc ccatt 1125

```

<210> 163

<211> 423

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (390)

<223> n equals a,t,g, or c

<400> 163

```

gggtcgaccc acgctgccga gatggcggtt cgcagcaaga ggccggagca cggcgggccc 60
ccggagctgt tttatgacaa gaatgaagcc cggaaatacg tgcgcaactc acggatgatt 120
gatgtccaga ccaaaatggc tgggcgagct ttggagctcc tttgtctgcc ggaggtcagc 180
cctgttacct cttggatatt ggctgtggtt ctgggctgag tggagattat ctctcggatg 240
aagggcacta ctgggtagc atcgacatca gccctgccat gctggatgcg gccttggacc 300
gagacactga gggagacctg cttctggggg acatgggcca gggcatcccc ttcaaaccag 360
kttcattgat ggatgtatca gcattctgcn aatcagtggc tctgtaatgc aaaccaagaa 420
gtc 423

```

<210> 164

<211> 1642

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1614)

<223> n equals a,t,g, or c

<400> 164

```

acccacgcgt cggcggtctg gcggagcaga acggattgca gggtcagcca tgtcatctga 60
gcctccccca ccaccacagc cccccacca tcaagcttca gtcgggctgc tggacacccc 120
tcggagccgt gagcgctcac catccctctc gcsgggcaac gtgggtccaa gccactgcc 180
cactcgccgg acgaggacct tctcgggcag ggtgcgggct tcacagggcc ccgtctacaa 240
aggagtctgc aaatgcttct gccggtccaa gggccatggc ttcattacc cagctgatgg 300
cggccccgac atcttctctg acatctctga tgtggaagg gagtatgtcc cagtgaagg 360
cgacgaggtc acctataaaa tgtgtccat cccacccaag aatgagaagc tgcaggccgt 420
ggaggtcgtc atcactcacc tggcaccagg caccaagcat gagacctgg ctggacatgt 480
catcagctcc taggagatgg tggaaagcacc ctttgtctg tgcttgagg agactttgcg 540
gggaggaggc agcagacact ggagatgaca ttcttcaca cgagacggg cttcagccgg 600
gcatggtccc tctcaagtat ctcttgagg aaggggtatg gggggcagg gtggggtgtg 660
gggtgttccc ggcatcagc acagcctatg accattgcaa caacctctca ccattgaag 720
agcattaaaa gcatttaaaa aggaragggt cccactgggt gctgagtggg ggttccaacc 780

```

```
ccatcccagg gagtggatca aggggtggtat ttctccagct gctcagacac atgggctcaa 840
cccacagaat ccctcttcct cctggagctg gagggcccag attcccagat ctggccccct 900
ggcagcctga cagggacctt gcgtgacttc tccaaggcaa atttccacct aagtggcccc 960
tgcgcctctc ctggggcctg ggcaaagcag ttttctaatt cttggcttgg ttggttctag 1020
gggagctggc ttgaagtggg kggggaaagg cgggggtggc ggtcttttga ttggacggat 1080
gttgccctttt ggtgcctttg cagtgggagg cggcatagct gcctgtcttg ggaagacagt 1140
tctcccagca ctcccacccc tgggcacagc aggctggtac tgggaggctg aaccctctt 1200
agagcctgac cttttcatct gccttctggt tgtgtgacca tcaactcaaca gccatttcac 1260
agcccctgta attatggcgg cggggggctg ggggtggtgg ggtgggaagg gcttgtggag 1320
aggacacagt ctttgtttta aaactttgtc ccgatccatc cagaaaagag taggtagctt 1380
gcacccctgac agcctggcaa agtcaagaaa gttgaaggag aaacatacct ttggagaggg 1440
ggttttcttt aaaactagtg ttaagaaatg cttagggtatt ttttttttct tatttttcat 1500
aactaaagct ttcaccaga gccggctctg tttgcacttt gctgccgaca ttgcaaactt 1560
tttggcaggg tgggagactg agtctcattc tgtcamccag gctggagtgc agtngcccga 1620
tctcagcttt actgcaacct ct 1642
```

<210> 165

<211> 1115

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (390)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (394)

<223> n equals a,t,g, or c

<400> 165

```
aggaatgccg agtactgcag gggctcccca gggagtatgt gaatgccagg cactgtttgc 60
cgtgccaccc tgagtgtcag ccccagaatg gctcagtac ctgttttggg ccggaggctg 120
accagtgtgt ggcctgtgcc catcaagtgg atggcgctgg agtccattct ccgccggcgg 180
ttcaccaccc agagtgatgt gtggagtatt ggtgtgactg tktgggagct gatgactttt 240
ggggccaaac cttacgatgg gatcccagcc cgggaggatc cctgacctgc tggaaaaggg 300
ggagcgggctg ccccagcccc ccatctgcac cattgatgtc tacatgatca tggtaaatg 360
ttggatgatt gactctgaat gtcggccaan atnccgggag ttggtgktg aattctccc 420
catggccagg gacccccagc gctttgtggt catccagaat gaggacttgg gccagccag 480
tcccttggac agcaccttct accgctcact gctggaggac gatgacatgg gggacctggt 540
ggatgctgag gagtatctgg taccacagca gggcttcttc tgccagacc ctgccccggg 600
cgctgggggc atggtccacc acaggcaccg cagctcatct accaggagtg gcggtgggga 660
cctgacacta gggctggagc cykctgaaag agggaggccc caggtctcca ctggcaccct 720
ccgaagggct ggctccgatg tattttratg tgacctggga atgggggcag ccaaggggct 780
gcaaagcctc cccacacatg accccagccc tctacagcgg tacagtgagg accccacagt 840
acccctgccc tctragactg atggctacgt tgccccctg acctgcagcc cccagcctga 900
atatgtgaac cagccagatg ttcggcccca gccccctcg ccccgagagg gccctctgcc 960
tgctgcccga cctgctggtg ccactctgga aaggsccaag actctctccc cagggaagaa 1020
tggggtcgtc aaagagttt tgcttttggg ggtgccgtgg agaaccocga gtattgacac 1080
cccaggggag ggagcttgcc cttcagcccc acctt 1115
```

<210> 166  
 <211> 1066  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (10)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (739)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (968)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1023)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1025)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1042)  
 <223> n equals a,t,g, or c

<400> 166  
 gggcacgagn cacctgagcc ccttgtctcg caccggctcc caggagggca cctccatgga 60  
 gggctcccgc cccgtgccc ctgccagagc caggcaccct caagaccagt ctggtggcta 120  
 ctccaggcat tgacaagctg accgagaagt cccagggtgc agaggatggc accttgcggt 180  
 ccctggaacc tgagccccag cagagcttgg aggatggcag cccggctaag ggggagccca 240  
 gccaggcatg gagggagcag cggcgaccgt ccacctcatc agccagtggg cagtggagcc 300  
 caacgccaga gtgggtcctc tcctggaagt cgaagctgcc gctgcagacc atcatgaggc 360  
 tgctgcagggt gctggttccg cagtggagaa gatctgcac gacaagggcc tgacggatga 420  
 gtctgagatc ctgcggttcc tgcagcatgg caccctggtg gggctgctgc ccgtgcccc 480  
 ccccatcctc atccgcaagt accaggccaa ctcgggcact gccatgtggt tccgcaccta 540  
 catgtggggc gtcattctatc tgaggaatgt ggacccccct gtctggtacg acaccgacgt 600  
 gaagtctgtt gagatacagc ggggtgtgagg atgaagccga cgaggggctc agtctagggg 660  
 aaggcagggc cttggtccct gaggttccc ccatccacca ttctgagctt taaattacca 720  
 cgatcagggc ctggaacang cagagtggcc ctgagtgtca tgccctagag acccctgtgg 780  
 ccaggacaat gtgaactggc tcagatcccc ctcaaccctc aggctggact cacaggagcc 840

ccatctctgg ggctatgccc caccagagac cactgcccc aacactcgga ctccctcttt 900  
aagacctggg ytcagtgtg gcccctcagt gccaccact cctgtgttac ccagccccca 960  
gaggcagnaa rccaatgggt cactgttgcc cctaaagggg ggtttttgaa ccaaggggga 1020  
aancnacggg gcctgggtcc cntttggaaa ggtttcccct gggaaa 1066

<210> 167

<211> 657

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (278)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (564)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (597)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (602)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (635)

<223> n equals a,t,g, or c

<400> 167

gtcgcgagcg ctgccgtcgg gaggcgctcc gaggttcgag gctgtgcccc gcgaccccg 60  
cttcggcgct cggctcgcag gatggatccc gtaccgggga cagactcggc gccgctggct 120  
ggcctggcct ggtcgtcggc ctctgcaccc ccgcgcggg gkttcagcgc gatctcctgc 180  
accgtcgagg gggcaccgcc agctttggca agagcttcgc gcagaaatct ggctacttcc 240  
tgtgccttag ttctctgggc agcctagaga acccganga gaacgtggtg gccgatatcc 300  
agatcgtggt ggacaagagc cccctgccgc tgggcttctc ccccgctcgc gamcccatgg 360  
attccaaggc ctctgtgtcc aagaagaaac gcatgtgtgt gaarctgttg cccctkggar 420  
ccamggacac ggctgtgttt gatgtccggc tgagtgggaa gaccaagaca gtgcctggat 480  
accttcgaat aggggacatg ggcggtttt ccatctggtg caagaaaggc caaggccccc 540  
aggccagtgt cccaagccc cgangtcctc agcccgggac atgcaagggc ttctctntgg 600  
angcagccag ccagcccaag ttaagggcgg gcctncttgg aagccggaca agcgttc 657

<210> 168

<211> 1026

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1011)

<223> n equals a,t,g, or c

<400> 168

```

ggcacgagga gagatggagg ggcggcaggt gctggaggtc aagatgcagg tggagtacat 60
gtcattcagc gcacacgcgg acgccaaggg catcatgcag ctggtggggc aggcagagcc 120
gkagagcgtg ctgctggtgc atggcgaggc caagaagatg gagttcctga agcagaagat 180
cgagcaggag ctccgggtca actgctacat gccggccaat ggcgagacgg tgacgctgcc 240
cacaagcccc agcatcccc taggcatctc gctggggctg ctgaagcggg agatggcgca 300
ggggctgctc cctgaggcca agaagcctcg gctcctgcac ggcaccctga tcatgaagga 360
cagcaacttc cggtggtgt cctcagagca agccctcaaa gagctgggtc tggctgagca 420
ccagctgcgc ttcacctgcc gcgtgcacct gcatgacaca cgcaaggagc aggagacggc 480
attgcgcgtc tacagccacc tcaagagcgt cctgaaggac cactgtgtgc agcacctccc 540
rgacggctct gtgactgtgg agtccgtcct cctccaggcc gccgcccctt ctgaggaccc 600
aggcaccaag gtgctgctgg tctcctggac ctaccaggac gaggagctgg ggagcttctt 660
cacatctctg ctgaagaagg gcctccccc ggccccagc tgaggccggc aactcaccca 720
gccgccacct ctgccctctc ccagctggac agaccctggg cctgcacttc aggactgtgg 780
gtgccctggg tgaacagacc ctgcaggctc catccctggg gacagaggcc ttgtgtcacc 840
tgctgcccc ggagctgtt tgagctgaa gaaacaaact ggtctccagg ctgtcttgcc 900
tttattcctg gttagggcag gtggtcctag acagcagttt ccagtaaaag ctgaacaaaa 960
aaaaaaaaaa aaaaaattgg gggggggccc gttaccatt tggcctttag ngggggtttt 1020
aaatta                                     1026

```

<210> 169

<211> 774

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (730)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (733)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (754)

<223> n equals a,t,g, or c

<400> 169

```

ggcataaaca tcgggtggtg ttcagatcct gctgccggca gctcgaggct aggatggctg 60
gagatgtgag ggcctttgtc tcatcacatc cgagcacagc tcagcaagat gctcttagct 120
agraaacaga tttatgtgt taatgttaaa aattttgcag ttatttatct tgtggatatt 180

```

```
acagaagtgc ctgacttcaa caaaatgtat gagttatacg atccatgtac tgtcatgttt 240
ttcttcagga acaagcacat catgattgac ttggggactg gcaacaacaa caagattaac 300
tgggccatgg aggacaagca ggagatggg gacatcatcg agacgggtga ccgcggggcc 360
cgcaaargcc gcggcctggg ggtgtccccc aaggactact ccaccaagta ccgctactga 420
ggcgccctca gtctgcgcgg ataaatgtcg tggagccctt tttgtatgga aacgttttaa 480
gctattttaa gcctttggaa aatacaggaa gctccagggc tggagcacct ctgagatgga 540
attgataaca tgggtcttaac tcaccgaaat aaacaagcac gtggtgagag gagcaggcct 600
acttgtttgt tctcaggaaa cttaatgaat agattactga ttttcctagt caaagttaat 660
tcttaccctt ggagtaaaac gaagggtgtt atcctgtgag cctgtgcgtt ttgcatactg 720
ggttggtttn ctngggcttc ggtgacagca tatnccgcga gctgggcttt aaca 774
```

&lt;210&gt; 170

&lt;211&gt; 402

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 170

```
ggcacgagcg gcggtggggc ggacagccgg ggtgcgcact tgggcccccc tggccatggc 60
ggcgaagggt gacctgagca cctccaccga ctggaaggag gcgaaatcct ttctgaaggg 120
cctgagtgac aagcagcggg aggaacatta cttctgcaag gactttgtca ggctgaagaa 180
gatcccgaca tggaaggaga tggcgaaagg ggtggctgtg aagggtggag agcccaggta 240
taaaaaggac aagcagctca atgagaaaat ctccctgctc cgcagcgaca tcaccaagct 300
ggaggtggac gccatcgtca acgcccga cagctccccg ccccgagga gcctaattaa 360
agatcttcgt tgtggcaaaa aaaaaaaaaa aaaaaaaaaa aa 402
```

&lt;210&gt; 171

&lt;211&gt; 796

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 171

```
aggcatcggg gacagccgct gcggcagact cgagccagct caagcccga gctcgcaggg 60
agatccagct ccgtcctgcc tgcagcagcc caaccctgca caccaccat ggatgtyttc 120
aagaagggtt tctccatcgc caaggagggc gtggtgggtg cgggtgaaaa gaccaagcag 180
ggggtgacgg aagcagctga gaagaccaag gaggggttca tgtatgtggg agccaagacc 240
aaggagaatg ttgtacagag cgtgacctca gtggccgaga agaccaagga gcaggccaac 300
gccgtgagcg aggtgtggt gagcagcgtc aacactgtgg ccaccaagac cgtggaggag 360
gcggagaaca tcgcggtcac ctccggggtg gtgcgcaagg aggacttgag gccatctgcc 420
ccccaacagg aggtgtaggc atccaaagag aaagaggaag tggcagagga ggcccagagt 480
gggggagact agagggttac aggccagcgt ggatgacctg aagagcgtc ctctgccttg 540
gacaccatcc cctcctagca caaggagtgc ccgccttgag tgacatgcgg ctgcccacgc 600
tcctgccctc gtctccctgg ccacccttgg cctgtccacc tgtgctgctg caccaacctc 660
actgccctcc ctcgccccc cccaccctct ggtccttctg accccactta tgctgctgtg 720
aatttttttt ttaaatgatt ccaaataaaa cttgagccca ctyctaaaaa aaaaaaaaaa 780
aaaaaaaaag gggccc 796
```

&lt;210&gt; 172

&lt;211&gt; 478

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 172

```
aattcggcag agcctggttg cagggcagct aggggtctct gcattctcca catggtctca 60
tgcccccttt tgtcccttac aggaggactt gaggccatct gcccccaac aggaggggtga 120
ggcatccaaa gagaaagagg aagtggcaga ggaggccag agtgggggag actagagggc 180
tacaggccag cgtggatgac ctgaagagcg ctctctgccc ttggacacca tccctccta 240
gcacaaggag tgccgcctt gagtgacatg cggctgccc cgtctctgcc ctgctctccc 300
tgggcaccct tggcctgtcc acctgtgctg ctgcaccaac ctactgccc tccctcggcc 360
ccaccacccc tctggtcctt ctgacccac ttatgctgct gtgaattttt tttttaaatg 420
attccaaata aaacttgagc ccactcctaa aaaaaaaaaa aaaaaaaaaa aaaaaaaa 478
```

&lt;210&gt; 173

&lt;211&gt; 656

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (59)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 173

```
tttcccaatg cctgccacca cggagactca gggccacctg ccaccctccc tcgtgcct 60
ctgcccttgg gatggggcgc tcctgaatgt acgtgggccc cgggtgtttac aaggaggtga 120
tcactacaaa cctctgccag aagcaggtgg tggagaagat accactgccc ttttttgcca 180
tgtccctgag cctgtccccc gggaccaccc tcctggctgt tggttttgcg gagtgcctgc 240
tgaggctggt agactgtgcc atggggactg cccaagactt tgccggccac gacaacgcag 300
tgcacctgtg caggttttaca cktccgcca ggctgctctt caccggccgc cgcaacgaga 360
tccttggtgt ggaggtcccc ggctctgag atgcagcagg gactgtggtg gtgggcatca 420
acgcctggtc atgccaggca cctggacaca ggcttgccag aggcgccagg ttgtcaatgg 480
cctcatgctg ggacaggcca ggattcacgt aaatcgctg gagcaagctg ttgtaaattt 540
ggcgccctgt gaatactttc atacctgtt cccttttgcc taagaaatct ttaatgtttc 600
tatcttgtaa taaacatggg catttattgc aaaaaaaaaa aaaaaaaaaa aaaaaa 656
```

&lt;210&gt; 174

&lt;211&gt; 1891

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 174

```
gagccccctc cgagagggga gaccagcggg ccatgacaag ctccaggctt tggttttcgc 60
tgtgtctggc ggcagcgttc gcaggacggg cgacggccct ctggccctgg cctcagaact 120
tccaaacctc cgaccagcgc tacgtccttt acccgaacaa ctttcaattc cagtacgatg 180
tcagctcggc cgcgcascgg gctgtcagc cctcgacgag gccttcacgc gctatcgtga 240
cctgcttttc ggttcggggt cttggccccc tccttacctc acagggaac ggcatacact 300
ggagaagaat gtgttggttg tctctgtagt cacacctgga tgtaaccagc ttcctacttt 360
ggagtcatgt gagaattata ccctgacctt aaatgatgac cagtgtttac tcctctctga 420
gactgtctgg ggagctctcc gaggtctgga gacttttagc cagcttggtt ggaaatctgc 480
tgagggcaca ttctttatca acaagactga gattgaggac tttccccgct ttcctcaccg 540
gggcttgctg ttggatacat ctgcaccata cctgccactc tctagcatcc tggacactct 600
ggatgtcatg gcgtacaata aattgaacgt gttccactgg catctggtag atgatccttc 660
cttcccatat gagagcttca cttttccaga gctcatgaga aaggggctcct acaaccctgt 720
```

```
caccacacatc tacacagcac aggatgtgaa ggaggtcatt gaatacgcac ggctccgggg 780
tatccgtgtg cttgcagagt ttgacactcc tggccacact ttgtcctggg gaccagktat 840
ccctgggatt actgactcct tgctactctg ggtctgagcc ctctggcacc tttggaccag 900
tgaatcccag tctcaataat acctatgagt tcatgagcac attcttctta gaagtcagct 960
ctgtcttccc agatttttat cttcatcttg gaggagatga ggttgatttc acctgctgga 1020
agtccaaccc agagatccag gactttatga ggaagaaagg cttcgggtgag gacttcaagc 1080
agctggagtc cttctacatc cagacgctgc tggacatcgt ctcttcttat ggcaagggct 1140
atgtgggtgtg gcaggagggtg tttgataata aagtaaagat tcagccagac acaatcatac 1200
aggtgtggcg agaggatatt ccagtgaact atatgaagga gctggaactg gtcaccaagg 1260
ccggcttccg ggcccttctc tctgccccct ggtacctgaa ccgtatatcc tatggccctg 1320
actggaagga tttctacgta gtggaacccc tggcatttga aggtaccctt gacagaagg 1380
ctctgggtgat tgggtggagag gcttgtatgt ggggagaata tgtggacaac acaaacctgg 1440
tccccaggct ctggcccaga gcargggctg ttgccgaaag gctgtggagc aacaagttga 1500
catctgacct gacatttgcc tatgaacgtt tgtcacactt ccgctgtgag ttgctgaggc 1560
gaggtgtcca ggcccaaccc ctcaatgtag gcttctgtga gcaggagttt gaacagacct 1620
gagccccagg caccgaggag ggtgctggct gtaggtgaat ggtagtggag ccaggcttcc 1680
actgcatcct ggccagggga cggagcccct tgccttcgtg ccccttgcct gcgtgcccc 1740
gtgcttgag agaaaggggc cgggtgctggc gctcgcattc aataaagagt aatgtggcat 1800
ttttctataa taaacatgga ttacctgtgt ttaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa g 1891
```

<210> 175

<211> 2161

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2153)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2160)

<223> n equals a,t,g, or c

<400> 175

```
cgcttccgtc cacttggcga gtgagacgct gatgggagga tggacrtact ggtgtctgag 60
tgctccgcgc ggctgctgca gcaggaagaa gagattaaat ctctgactgc tgaatttgac 120
cggttgaaaa actgtggctg tttaggagct tctccaaatt tggagcagtt acaagaagaa 180
aattttaaaat taaagtatcg actgaatatt cttcgaaaga gtcttcaggc agaaaggaac 240
aaaccaacta aaaatatgat taacattatt agccgcctac aagaggctctt tggatcatgca 300
attaaggctg catatccaga tttggaaaat cctcctctgc tagtgacacc aagtcagcag 360
gccaaagtgt gggactatca rtgtaatagt gctatgggta tttctcagat gctcaaaacc 420
aaggaacaga aagttaatcc aagagaaatt gctgaaaaca ttaccaaaaca cctcccagac 480
aatgaatgta ttgaaaaagt tgaaattgct ggtcctgggt ttattaatgt ccacttaaga 540
aaggattttg tatcagaaca attgaccagt cttctagtga atggagttca actacctgct 600
ctgggagaga ataaaaaggt tatagttgac ttttcctccc ctaatatagc taaagagatg 660
catgtaggcc acctgaggtc aactatcata ggagagagta taagccgcct ctttgaattt 720
gcagggtatg acgtgctcag gttaaatcat gtaggagact gggggacmca gtttggcatg 780
ctcatcgctc acctgcaaga caaatattcca gattatctaa cagtttcacc tcctattggg 840
```



gatcttcagg tcttttataa ggaatctaag aagaggtttg atactgagga ggaatttaag 900  
aagcgagcat atcagtgtgt agttctgctc cagggtaaaa acccagatat tacaaaaagct 960  
tggaagctta tctgtgatgt ctcccgccaa gagttaaata aaatctatga tgcattggac 1020  
gtctctttta tagagagagg ggaatccttc tatcaagata ggatgaatga tattgtaaag 1080  
gaatttgaag atagaggatt tgtgcagggt gatgatggca gaaagattgt atttgtccca 1140  
gggtgttcca taccattaac catagtaaaa tcagatggag gttataccta tgatacatct 1200  
gacctggctg ctattaaaca aagactatct gagggaaaag cagatatgat tatctatgtt 1260  
gtggacaatg gacaatctgt gcacttccag acaatatttg ctgctgctca aatgattggg 1320  
tggtatgacc cttaaagtaac tcgagtcttc catgctggat ttggtgtggg gctaggggaa 1380  
gacaagaaaa agtttaaaac acgttcgggt gaaacagtgc gcctcatgga tcttctggga 1440  
gaaggactaa aacgatccat ggacaagtgt aaggaaaaag aaagagacaa ggtcttaact 1500  
gcagaggaat tgaatgctgc tcagacatcc gttgcttatg gctgcatcaa atatgctgac 1560  
ctttcccata accggttgaa tgactacatc ttctcctttg acaaaatgct agatgacaga 1620  
ggaaatacag ctgcttactt gttgtatgcc ttactagaa tcaggtctat tgcacgtctg 1680  
gccaatattg atgaagaaat gctccaaaaa gctgctcgag aaaccaagat tcttttggt 1740  
catgagaagg aatggaaact aggccggtgc attttacggt tccctgagat tctgcaaaag 1800  
attttagatg acttatttct ccacactctc tgtgattata tatatgagct ggcaactgct 1860  
ttcacagagt tctatgatag ctgctactgt gtggagaaag atagacagac tggaaaaata 1920  
ttgaagggtg acatgtggcg tatgtccta tgtgaagcag tagctgctgt catggccaag 1980  
gggtttgata tccctgggaat aaaacctgtc caaaggatgt aatccttcat aggtttgaac 2040  
actgtgtgtt ttaccaaaag tgccattggc actgtttgct tttttacaat catgtggaca 2100  
caagcataag taaagaaaat ttgtcaacca gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2160  
a 2161

<210> 176

<211> 2411

<212> DNA

<213> Homo sapiens

<400> 176

gggatccctg ctaccactct gaatccgata ccgcttctct tagaccgtca ctgagacaac 60  
ggttacctg acaaccgagc ccgagaaccg gagccttacc atcaaacttc ggaaacggaa 120  
gccagagaaa aaggtagaat ggacaagtga cactgtggac aatgaacaca tgggcccgcg 180  
ctcatcmaaa tgctgctgta tttatgagaa acctcgggcc tttggcgaga gctccacgga 240  
aagtgatgag gaggaagaag agggctgtgg tcatacacac tgtgtacgtg gccaccgcaa 300  
aggacggcgt cgtgcaacc taggaccgac ccccaccacc cctccccagc ctctgaccc 360  
ttcccagccc cctccagggc caatgcagca ctaaatccct ctctcctcca gcattcctgt 420  
gtctgtctg ccctaaatgt atccatgtgg ctacttctcc agccccctcc ttccctctct 480  
tctgcctgat agagggaaga ggaagaggag gacgaacaga gatcctgaaa ttctgacttg 540  
ctgctatttc agaaccagc ctctgggtt tccccagtc tcatttttcc tccaataacc 600  
cacccttctc tctcgaggga tctaggcacc ttgggtccag tgtcttctt ttgttctcac 660  
tgccaaactg cctgtcctgg gatctagtta tcttggccct gcaactctca catgagtagc 720  
gaacacttaa attgggtttt caacagtccc agctttcact gccagggtcc cagtcagatt 780  
ccagggaattt gcgcctaac tttgcttgc aatcctggtt tagagctatc ccactaaaat 840  
atttaaatcct aattcttagt ccttgctgt gagatatgag gtcttacagg agacctcaga 900  
gtccccagcc cttctcctcc tgctaaccct tctcacaccc tcaagaggag ttagaaaaga 960  
ggtccttgtc attctcacct cttatggaaa atggaataag aaataatcat atcctttctt 1020  
cccacccttc tcctgttatt taggatttct gacaaagctg gcttgagatt ggtcacttag 1080  
agccgactgt ctctctgcc tttgttttt cagcttcaga gacagatcca atatagtccc 1140  
agggacctg gtctctggga gaggaaggaa gagggaggga gcaaagagat tggggtatgt 1200  
cccctgtagt acactcttac ctcttacttc ctgactttg atttctccgg cagcccagat 1260

```

gttcagttct cttggccct ctctaccct tactgggatc tggttttcat tttccgggtcc 1320
ttttgccata cacagttaca gagatcagtc aaatccatac caccactgag atctcattta 1380
ttgccacaga tgcacaaaat aaataaccca aaatcacaaa atgtgttaaa tatgggcccc 1440
tttatactta tggggaaggg tktkagactw twcacaagga tgarthttgga ratktctgaa 1500
gtattcccag gttkaggarg agagagggga aatagcacca ttggttcctt tccgtgagta 1560
tgtgcgggga gaagtttcaa gaaggttctt atggaaaaaa ggctgtgagc atagaaagca 1620
gtcataggag gttggggaac tagcttggtc cccccaccc ccagatcctg caaaagaggt 1680
acaaagcttc ccagaggcca cagggccaga ccagagtcaa gcctcttggt ttaggagaaa 1740
cctcagtgga caggcagggt agcccagtc ttagatctgt kgggaaggcc ctgagccctt 1800
ctggagctag gagtggcaag agtgggagtc aagtatttga ccagcagagc ctctatgtag 1860
gaatcatggt cactttacca atactgatgg ggagggcctg tccccattg caggcctaga 1920
atggtttgaa tgggagaagt caggaagtac tgtagtagct gtaggggaga gaagattctg 1980
agagccagaa ggcmwsgaat ggatttggt ttgagcaggg acgtggaaac gtggagacca 2040
ggtgaggtct cattattttg gggcgaaaat gtgggttgct attaatactc ctgcaatggg 2100
cgtgtgaatg tgttcccaga aatgagtggg gaattccacc cccaaaaagc agctgcaggg 2160
ccagtgcagg gccaaacttc tagttggaga cgagactcag ctttccgctg gtacaatgcg 2220
gacggagcac gaggtgcga ggtgcagaac agcgggaaga tgcgctcccc agggggccag 2280
ggcctggaag gtaaagcagg tcgagtgagc ggccgtcgta gagagccacc ggccccgctc 2340
ccagtccagg tccamcgaa atgccgcggc gggggctcaa caccgcccag cagggtgggt 2400
tcgggtgccg t 2411

```

<210> 177

<211> 1338

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1234)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1276)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1289)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1326)

<223> n equals a,t,g, or c

<400> 177

```

ggcacgagaa aaaactcaga aatgctaagt gtacttattt gttgaagaaa cttgttacat 60
attactaaca tctttttttt ttatgagaaa tacttttccc ataaccacaaa aattcagtga 120
gcagaatggc cttgcttgag gtttttgcaa atctctcggg tgtctggctt agtgggaggc 180
agctgggccc tcatacctgc ctccgcactt cagctgtttg acataaaccc agcttcgtgt 240

```

```

gagtgaagg gaagggcctg gggaccctca gaggttctcg gaccacactt tgagaactcc 300
tcgtctggaa gacaggcctg gggatgccat gtggggtgag ggcttacggg cttggtgtcg 360
ctttgtggag aaccgctggt gtctgaagcg ggtgtcagcc cactgcacc ttggtcttct 420
gggtgtcct gatgccgagg ccacttccc agccatgctg actttgcctc tttcccctcc 480
cagcagaaaa atggctacaa acttcctagc acatgagaag atctgggtcg acaagttcaa 540
atatgacgac gcagaaagga gattctacga gcagatgaac gggcctgtgg caggtgcctc 600
ccgccaggag aacggcgcca gcgtgatcct ccgtgacatt gcgagagcca gagagaacat 660
ccagaaatcc ctggctggaa gctcaggccc cggggcctcc agcggcacca gcggagacca 720
cgtgtgagtc gtcgtccgga ttgccagtct ggaagtggag aaccagagtc tgcgtggcgt 780
ggtacaggag ctgcagcagg ccattctcaa gctggaggcc cggctgaacg tgctggagaa 840
gagctcgcct ggccaccggg ccacggcccc acagaccag cactatctc ccatgcgcca 900
agtggagccc ccagccaaga agccagccac accagcagag gatgacgagg atgatgacat 960
tgacctgttt ggcagtgaca atgaggagga ggacaaggag gcggcacagt tgcgggagga 1020
gcggytamgg caktacgcgg agaagaaggc caagaagcyt gcaytgggtg ccaagtcctc 1080
catcctgtcg gatttcaagc cttggggatg atgagacgga catggctcag ctggaggcct 1140
gtgtgcgctc tatccagctg gacggctggt ctggggggct tccaagctgg tgcctgggc 1200
tacggttatc cgaagctaa caatttcattg tgnngttgga ggacgacaag tgggggacaa 1260
cttgcgtggag gagganttca ccatttttna ggagcactgc aattttcaa tcgcattttt 1320
caacanattt gaagcccc 1338

```

&lt;210&gt; 178

&lt;211&gt; 1614

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1213)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 178

```

tgcatgtggt acatcccttc ttctcatcc tcttcatgta cttcaccggc tgctttactg 60
cctctaaagc tgagagcttg attccagggc ctgccctgct cctggtggca ccagtgggc 120
tgtactactg gtacctggtc accgagggcc agatcttcat cctcttcac ttacaccttc 180
tcgccatgct ggcctcgtc ctgcaccaga agcgaagcc ccttctcctg acagcaacgg 240
cctcttcctc ttctcctcct tcgcactgac cctcttgctt gtggcgctct gggtcgctg 300
gctgtggaat gaccctgttc tcaggaagaa gtaccgggt gtcactacg tccctragcc 360
ctgggctttc tacacccttc acgtcagcag tcggcactga gtccctggca ccaggctctg 420
gcgctctgct ggggtggagg gtgggcatg gagggcatct gaatacagga gtagggggg 480
tgtgggtgtg taaccagaga ccgagagcat gagggggtg tgctcgtgt gcgtggattc 540
gtgtgtgtgt gtgtgtcttg tatatgtgtg cgcagagtgc atcattttca gactctacta 600
tttccgtcaa gtttctgttt gatttggatc atctcaggat cggattctgt ttagagtgt 660
ttctgggcca ggatccgggc ccctgccctc ctctgcacct gaccacactc cctactcagg 720
gctagtctgt tcttcccgga catcttctgg tagccgtgca ggagagggct ggggtgggca 780
gaggccagga ggggacctgg tgtgtcacct gccaccacc tggctcatcc ctcaggccca 840
ccctgacctt acattacata ggttacgtca gcctactgtg gctgttgagc aaagcatttc 900
tcctttctg gctcatttg cactagatgg gcctgtggc ccaaagtagg tcagtaggtt 960
ggggttgctg acacccttg ggtgcagctt tgggacagat gagggtctt gtcctgtcac 1020
tgccctctcc ctgcctggg gctatgtgca ctccagaccc ctgcccaggc tcaggcccat 1080
gaggtatgga gacaccctgg cccccaggag ctggaggcac cggccactcc cctggcattc 1140
cagctttgca ggtgacctc ctctacccaa agctctgtcc ccctgctccc actccagaag 1200

```

```
aactgcggca cgngettcgg gcagcctagc cacaggcttt gagcgctgc attcctgggg 1260
gctggagggt ggggtgccaa aggccctgag caaaagccag agctcctctc atcaaagcct 1320
ttacaagggtg ctggggcccag aggctttgcc ttgacagagt ggcccagggt ttcaagggtg 1380
gaggaacctc cccctaccta ggacccttcc tgtgggggggt ctacagagtc agggacagaa 1440
gggaagggtg ccacaggaag tcacagtggg gccagggat gtgtcagccc ccagccacgg 1500
ggacgcggga ttcaagaatg aagtaaatac agtcacagcc ccaaaaaaaaa aaaaaaaaaa 1560
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 1614
```

<210> 179

<211> 4292

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (654)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (4288)

<223> n equals a,t,g, or c

<400> 179

```
ggaaggtcca gagggggcaa acctctttat ttaccacctt ccacaggaat ttggagacca 60
ggacattctg cagatgttca tgcccttttg aaatgttatc tctgctaaag tcttcattga 120
caaacagacc aatctgagca agtgcttttg ttttgtttagc tacgacaatc cagtctctgc 180
acaagctgct atccaagcta tgaatggctt tcagatcggc atgaaacgct tgaagggtga 240
gctgaagcgt tccaaaaacg acagcaaacc ttactgatcc taaccccaga ggctccctgc 300
tctcatttta gctttcttag gacatcttca tgcccgttag ttcatcgttt gcctagcatg 360
tccctgtggc gtctcaaaaa aaagtttcat cgtcccgtca ttgtttctga tgtctttctg 420
acctcacatc atatttggtt ctccactga cctttgatct agtttgacct ttgaaatttg 480
catgtgacct catctagcta tgaattctgg gaagtcaatg tgaaaaacat tgcgtcatc 540
atgcaagact gaaatttatt attagacaaa ttcattatag aaaaaacctg tggcaaaaac 600
gtttctttct tatttttttt cttttcctaa aacagacttg aaagtattat acangggatt 660
ggcattcttc ccggtcactg gtaacaatag caatatgtgt ccagggacac agaattgttg 720
tttctaacag actacttcca aaaacagttt gagaaaaaaaa ctgtctgatt ttaagtctct 780
agaggtctgt aatagttttt acatttttca ggcagtgtaa agttttttga taaggccatt 840
ttaggtggct cactttctca ttaagatata tatatagaac cactttttgt agattagtat 900
aagaaaaata tttaccctgt tttggggcaa atgctacctt tttgtgtcac cttttgtgta 960
actcacagtt agacaatcca tgggttaatg cacatgaaat tacctatatt ttatactgtt 1020
tcaatgtaca ggagaaagggt tactgtaaac tgtgttatgt tgggtgcttct gtgaattaa 1080
ttgtggtttc atcatgagtc ttaatgttct ttgttgataa gacaagttta gaattggttt 1140
acttaataca aaaaaaaaaa aaagaatttc aaaaaaaaaa gttgtttgct taaaaaaaaa 1200
ttcatgtgag ggaaaaaaaa aaaacctatt ccagaataag ttttgtgttg gcttgtgaag 1260
cattgatgtc atttttttta attgtggact atttagatgt gtttgtgttc agcaaaatgt 1320
gactctgttt tttcttttaa agaaaaaaag tgaaaatata tagtgccaaa ttccaaagggt 1380
acttccttcc tagagcttca gtgtgtttct tgtgagaagt aatttgataa catgggtatt 1440
ttattatgtg ttttgtataa atccctaata tttaaaaaaa aaaacaaaac aaaaaaagggt 1500
tacaaagttt gttaacttgc tatcctgtgg tcttgttgcc tgaaattgtt attgtttgtt 1560
atttctctct gatgtttttt gtaagacatt gtataagtc ccatgtccca cttttttaac 1620
```

```

cactccgcac atcagtgtctg tgaaggcaac ctcaccatgt attttcttca taatctatgg 1680
aaacctctaa ggtgagaaag ttttgaactt ttaacccttt ctaccagag ctatctggaa 1740
tggtgatgac tttttatact gtcatgattt gagtttgttt tggggtgttt ccaatttgga 1800
tttttttccc tgcatctatc ctctaagttg tttcggtttg actactttgt tctttggtta 1860
agatccaaaa gaaaacagaa aacaattcca cgaggccaat ctaaaggga aaaatcctac 1920
actactttta ctacttttga ttatttctca tttttgggaa aagaattcct aatgtgctac 1980
tagaattcct tcttcagttt taacgagtaa ttggataaac cctgagggaa aacggaggta 2040
gattcagcac ctaacaatcc tgtatgcttt tgagatcacg tttagtgtta tgccttagtc 2100
tagaatattt tcatatacct tgcagtaaaa cgactttgtg gcaggacagt ctcttgaggg 2160
gttttgtttc tgtttcctaa atactcctaa ataataattc taatcagcca ttatgctggg 2220
gcatctctga tcccagtagg tacctctgaa tataccagggt gtctggagtt agaagcccat 2280
agccctttcc cagccttttt ggttttttta attgaacaca tttcatctaa gtaaagctca 2340
gttctttatc acaatttact gaccaaatac ctgacaccag ttctgtctgc cactttttta 2400
agtgccatat gactttctac gaacaggtag cttgtgtgct tgacaaatcc taatgtcacg 2460
cctacagccc caacacaagc tccagtcttc ctcttcggca tgccctggaa gcttcttggc 2520
ctcagctccc ctccccgct cagcaccctg ttaggatcag tgtgtgtgga tgggtagacc 2580
ctgggatgga aaggactagc ctctactgat gcaaaaaaac aaaaagcaac acaaacgttt 2640
ccttcttata gcacatgcac ttccttaca tgacatgatt tgtattatcc tcacatgtgt 2700
ttactactgc tggggccttc ctctatctc tgagggtat tttgtacttt ctgcagcaat 2760
cagcttaata acaacactta ttgcacctgt ctctctctga gaacacggtg tgtctcgaca 2820
cgtaccacgt acgtggaaac acaagagccc accacttgaa tttctaagac catttcattc 2880
tgaaacttct tatcaattac ctaaatctca acgaaaaaca atttactgaa gccgactccc 2940
ctccccatct ccctctcaac ctcaaccac ctgcatgcat ctccccaga ggaaacactg 3000
agggtagggg acaggaggct caggacgcgc cctctgaatc gagtgtttct tcttcacaag 3060
tcaccaagag aggacatgag ggggaaagtc cttttttgcc ctctccaaa aaataacctt 3120
ccacagagac aaactgtcct tctatccact tttatctttt aataaatatc aaaaggaaaa 3180
agctgcaagg gtgcaaagg cctgtgccag aagaaaacac acacaggga accgcttttt 3240
ttaatcaatt gtagagaata gtcattttta atctaaatta gagaattgtg atacaatggc 3300
agtcctcaaa ggcgtaacga gttcatcttt ctttcacatc aggggttata gttggcttgt 3360
gtactctctg aatcattttta ctgtttgttt ttattatctt aagtgtctat taaaaaaaaa 3420
aaaaatttta aaaaacctgt agtttcatta ctttttgaa taatgtcata caaaaaatgt 3480
atttgttttt ttgtgctgtg agaattgatg tttgtagatt aataatcatt ttgtttagaa 3540
ttacaaaata gtttttaaat attgtctgag aaaagccaaa gttaatgcaa cctagtggaa 3600
actgtaagac catttgagta ttgtttgtt tattgatgca tttggatttt gttgtttgat 3660
ggaatttgag ccaaaaaaaaa aatacgcagg ctctcctatt tctacaactg attgtactta 3720
tgcattttgt accagtggaa ctttttatac tggagattaa aaaaaaatg gaaatttttg 3780
tggtctgtct tgggtggccc ctgacaatga ctgatttcaa gtttgatttc ggggtgattg 3840
attgattgat tgatagaaaag aaagtgtctt ttcttttgag aattaaaaac tttggcttga 3900
tttctttttt ccctttgctt atatctagca ttagaatttt gtcttaaaat aacagcggta 3960
agtttcactt tttattctgt attgtgcagt tacacaataa ggtaattaga tttagaagta 4020
ctcagtcact ttaagtggat aatgtatta gttaaaactt tagggtttgc ttttttgctg 4080
tttagatcaa agttttttct gattcttctg tcctcattgt gaacataacc gtgtagttag 4140
aacagtcaaa cttatttttg taatgtatgt tattgtgtga tgcagttttt tgcttctgtc 4200
tccaatatta aaccattttc ctaataaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4260
aaaaaaaaaa aaaaaaaaaa aaaaaanaa aa
4292

```

&lt;210&gt; 180

&lt;211&gt; 243

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<220>

<221> misc feature

<222> (235)

<223> n equals a,t,g, or c

<400> 180

```
tcgacccacg cgcccggaga aggtgggctc tgggggggtcc tctgtgggca gcgggggatgc 60
cagctcctcr cgccatcacc atcgccgccc cgggttccac ctrccccaac agcccctgct 120
ccagagggaa gtgtggtgtg tgggcacaac gggaaacgct aaccaggcac agagctcaac 180
ggagcagaca ctgctgaagc ccaagtgaga aaccacggcg ctttggcgtg taacntggaa 240
tat 243
```

<210> 181

<211> 813

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (266)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (723)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (726)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (738)

<223> n equals a,t,g, or c

<400> 181

```
aattcggcag agaccaggtg tacctgagct acaataacgt ctccctccttg aagatgcttg 60
tggccaagga caactgggtg ctgtcctcgg agatcagtca ggtccgcctg tacactctgg 120
aggatgacaa gttcctctcc ttccacatgg agatgggtgg gcattgtggat gcagmccagg 180
ccttcctgct gctctcggac ctgmgtcaga ggccagagtg ggacaagcac taccggagcg 240
tggagctagt gcagcaggta gacranggac gacgccatct accacgtcac cagmcctgmc 300
ctcggagggtc acacaaagcc ccaggacttc gtgatcctgg cctcgaggcg gaagccttgt 360
gacaatgggg acccctatgt catcgcgctg aggtcgggtca cgctgcccac acaccgagag 420
acgccagagt acagacgcgg agagaccctc tgctcaggct tctgcctctg gcgcgagggg 480
gaccagctga ccaaggtagc ctgtagtaga ctcgggtcct gtccacagcc ctagctgcca 540
gcaatgctgt cctcacagag gcatagtcgc cccagctgg gttgtgctcc actgtgacgg 600
tggcccgggg ggaggtatgcc agcagcctgc ctatggytgc cagctgtgct gtgagcccag 660
cagcatggcc tgcattctggg aagggaacaca ggttggtccag agcccctggc acaactgctg 720
agncanatgc tgtggagnca gctgttacct tgtaagccac tggcccagca cctgcctaca 780
```

137

gggccagcct ggtggccaca gtgcacgtgg ggg

813

&lt;210&gt; 182

&lt;211&gt; 822

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (37)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (49)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (370)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (567)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 182

```

ggttttacat gaccgcagtc gccctcagtt tcaccngta ggaatcggnc tggggatgca 60
ccgtgctact ctcttcctcc aggccggtcc ccggcgctg cgcgcgatcc atgtccatgt 120
ccgcgcctat caataaagtt gctcacttgt tgccggcccc ctagmccgaa aggttgccg 180
cgcagmccga gaagtctcgc gatagccagc cgcggtgcc cttgcgcttc ccgagctggc 240
ggggtccgtg gtgcgggac gagattgcgg gctatggcgc cgaagttttt cgtcagtact 300
gggatatccc c gatggcacc gattgccacc gcaaagccta cagcaccacc agtattgcca 360
gcgtcgctgn cctgaccgcc gctgcctaca gagtcacact caatcctccg ggcaccttcc 420
ttgaaggagt ggctaagggt ggacaataca cgttactgc agctgctgtc ggggccgtgt 480
ttggcctcac cacctgcac agcgcctatg tccgcgagaa gcccgcacac cccctgaact 540
acttcctcgg tggctgcgcc ggaggcntga ctctgggagc acgcacgcac aactacggga 600
ttggcgccgc cgctgcgtg tactttggca tagcgccctc cctggtcaag atgggccggc 660
tggagggctg ggaggtgttt gaaaaaccca aggtgtgagc cctgtgcctg ccgggacctc 720
cagcctgcag aatgcgtcca gaaataaatt ctgtgtctgt gtgtgaaaaa aaaaaaaaaa 780
aaaaaaaaat yggggggggg cccskaacca attkccctta ag 822

```

&lt;210&gt; 183

&lt;211&gt; 1095

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1082)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1094)

<223> n equals a,t,g, or c

<400> 183

```
gcgcggaggc ggcgggcgag cctcctcctg ctgctgctgc gccccatccc cccgcgggcc 60
gccagttcca gcccgcaccc cgcgtcgggt cccgcgcccc tccccgggcc ccgccatggg 120
cctcaccgtg tccgcgctct ttctcgggat cttcgggaag aagcagatgc ggattctcat 180
ggttggttg gatgcggtg gcaagaccac aatcctgtac aaactgaagt tgggggagat 240
tgtcaccacc atcccaacca taggcttcaa tgtagaaaca gtggaatata agaacatctg 300
tttcacagtc tgggacgtgg gaggccagga caagattcgg cctctgtggc ggcactactt 360
ccagaacact cagggcctca tctttgtggt ggacagtaat gaccgggagc gggccaaga 420
atctgctgat gaactccaga agatgctgca ggaggacgag ctgcgggatg cagtgtgct 480
ggtatttgcc aacaagcagg acatgcccac cgccatgccc gtgagcgagc tgactgacaa 540
gctggggcta cagcacttac gcagccgcac gtggtatgtc caggccacct gtgccacca 600
aggcacaggt ctgtacgatg gtctggactg gctgtcccac gagctgtcaa agcgctaacc 660
agccaggggc agggccctga tgcccgaag ctctgcgtg catccccggg atgaccagac 720
tcccggactc ctacggcagt gccctttcct cccacttttc ctccccata gccacaggcc 780
tctgtctctg ctctgcctg catgttctct ctggtgttgg agcctggagc cttgtctct 840
gggcacagag ggggtccactc tcctgcctgc tgggacctat ggaaggggct tcctggccaa 900
ggccccctct tccagaggag gaggcaggat ctgggtttcc ttttttttt ctgttttggg 960
tgtactctag gggccagggt gggaggggga aggtgagggc ttcgggtggt gctataatgt 1020
ggcactggat cttgagtaat aaatttgctg tggtttgtaa aaaaaaaaa aaaaaacccc 1080
gnggggggcc ccgna 1095
```

<210> 184

<211> 3675

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2204)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3329)

<223> n equals a,t,g, or c

<400> 184

```
gcgagaaccg cctggagagc ctgccccgc agatgcgccg cctggtgcac ctgcagacgc 60
tcgtgctcaa tggaaacccc ctgctgcatg cacagctccg gcagctccca gcgatgacgg 120
ccctgcagac cctgcacctg cggagaccca gcgcacccag agcaacctgc ccaccagcct 180
ggagggtctg agcaacctcg cagacgtgga tctgtcctgc aatgacctga cacgggtgcc 240
cgagtgtctg tacacctctc ccagcctgcy ccgcctcaac ctcagcagca accagatcac 300
ggagctgtcc ctgtgcatag accagtgggt gcacgtggaa actctgaacc tgtcccga 360
tcagctcacc tcaactgccct cagccatttg caagctgagc aagctgaaga agctgtacct 420
```



```

gaattccaac aagctggact ttgacgggct gccctcaggc attggcaagc tcaccaacct 480
ggaagagttc atggctgcc aacaacaacct ggagctggtc cctgaaagtc tctgcaggty 540
cccaaagctg aggaacttg tcctgaacaa gaaccacctg gtgacctcc cagaagccat 600
ccatttctct acggagatcg aggtcctgga tgtgcgggag aacccaacc tggcatgccc 660
gccaagccc gcagaccgtg ccgctgagtg gtacaacatc gacttctcgc tgcagaacca 720
gctgcggcta gcgggtgcct ctcctgctac cgtggctgca gctgcagctg cgggagtggg 780
cccaaggacc ctatggctcg caagatgcga ctgcggaggc gcaaggattc agcccaggat 840
gaccaggcca agcagggtgct gaaggcatg tcagatgttg cccaggagaa gaacaaaaag 900
caggaggaga gcgcagatgc ccgggcccc agcggraagg tgcggcgttg ggaccagggc 960
ctggagaagc ccgccttgac tactccgagt tcttcacgga ggacgtgggc cagctgccc 1020
gactgaccat ctggcagata gagaacttcg tgctgtstct ggtggaggaa gccttccacg 1080
gcaagtctta cgaggctgac tgctacattg tgctcaagac ctttctggat gacagcggct 1140
ccctcaactg ggagatctac tactggattg gcggggaggg cactctgac aagaaagctt 1200
gctctgccat ccacgtgtc aacttgccga actacctggg tgctgagtg cgcactgtcc 1260
gggaggagat gggcgatgag agcaggaggt tcctgcaggt gtttgacaac gacatctcct 1320
acattgaggg tggaaacagcc agtggttctt aactgtgga agacacacac tatgtacca 1380
ggatgtatcg tgtgtatggg aaaaagaaca tcaagttgga gcctgtgccc ctcaagggga 1440
cctctctgga cccaaggtt gtttctctgc tggaccgagg gctagacatc tacgtatggc 1500
ggggggccca ggccacactg agcagacca ccaaggccag gctctttgca gagaaaatta 1560
acaagaatga gcggaaggg aaggctgaga tcacactgct ggtgcagggc caggagctcc 1620
cagagttctg ggagcactg ggtggggagc cctctgagat caagaagcac gtgcctgaag 1680
acttctggcc ccgcagccc aagctgtaca agtgggcctt gggttgggc tacctggagc 1740
tgccacagat caactacaag ctctccgtgg aacataagca gcgtcccaag gtggagtga 1800
tgccaagaat gcggctgctg cagagtctgc tggacacgcg ctgcgttaac attctggact 1860
gttggctcga cgtgttcac tggctcggcc gcaagtcccc gcgcctggtg cgcgtgccc 1920
ccctcaagct gggtcaggag ctgtgcggga tgtgcaccg gccacgcat gccacggtca 1980
gccgcagcct cgagggcacc gaggcgcagg tgttcaaggc caagttcaag aattgggacg 2040
atgtgttgac ggtggactac acacgcaatg cggaggccgt gctgcagagc ccgggtctct 2100
ccgggaaggt gaaacgcgac gccgagaaga aagaccagat gaaggctgac ctactgcgc 2160
tttctctgcc gcggcagccg cccatgtcgc tggccgaggg ggancagctg atggaggagt 2220
ggaacgaaga cctagacggc atggagggtt tcgtgctgga gggcaagaag tttgcgggc 2280
tgccggaaga ggagtttgcc cactcttaca cgcaggactg ctacgtcttc ctctgcaggt 2340
actgggtgcc tgtggagtac gaggaggagg aaaagaagga agacaaggag gagaaggccg 2400
agggcaaaga aggcgaggaa gcaaccgctg aggcagagga gaagcagcca gaggaggact 2460
tccagtgcac cgtgtacttc tggcagggcc gtgaagcctc caatatgggc tggctcacct 2520
tcaccttcag cctgcaaaa aagttcgaga gcctcttccc tgggaagctg gagggtgtac 2580
gcatgacgca gcagcaggag aacccaagt tcctgtccca tttcaagagg aagttcatca 2640
tccaccgggg caagaggaa gcggtccagg gcgccaaca gccagcctc taccagatcc 2700
gcaccaacgg cagcgcctc tgcaccggg gcatccagat caacaccgac tccagcctcc 2760
tcaactccga gttctgcttc atctcaagg ttccctttga gagtggagac aaccagggca 2820
tcgtgtatgc ctgggtgggc cgggcatcag accctgacga agccaagttg gcagaagaca 2880
tcctgaacac catgtttgac acctcctaca gcaagcaggt tatcaacgaa ggtgaggagc 2940
ctgagaactt cttctgggtg ggcatgggg cacagaagcc ctatgatgac gatgccgagt 3000
acatgaaaca cacacgtctc ttccggtgct ccaacgagaa gggctacttt gcagtgactg 3060
agaaatgctc cgacttttgc caagatgacc tggcagatga tgacatcatg ttgctagaca 3120
atggccaaga ggtctacatg tgggtgggga cccagactag ccagggtggag atcaagctga 3180
gcctgaaggc ctgccaggta tatatccagc acatgcggtc caaggaacat gagcggccgc 3240
gccggctgcy cctggtccgc aagggcaatg agcagcacgc ctttaccgc tgctccacg 3300
cctggagcgc cttctgcaag gcctggcnt aagacaggct ggcacagccc caggcttggg 3360
gaggaagagg aaggggcctc atccactgtc tgctagcaaa gaatgtactc aggtgacacc 3420
acctgtcca gccacgtcca gtgccacagt cccagtagc ctcaagcagc accaatgggg 3480

```

```
atgaccctga caggtgccct caggggtctg ggaaatccaa ctctctccac agtgtgagtg 3540
cacgtgtgaa gccccctcac tcttccgcta gggataaagc agatgtggat gccctttaag 3600
agatattaaa tgctttttatt ttcaatatta aaaaaaaaaa aaaaaagggc ggccsctcgc 3660
gatctagaac tagtc 3675
```

<210> 185

<211> 1040

<212> DNA

<213> Homo sapiens

<400> 185

```
ggacagagcc tccactgagc tgctgcctgc ccgccacata cccagctgac atgggcaccg 60
caggagccat gcagctgtgc tgggtgatcc tgggcttcct cctgttccga ggccacaact 120
cccagccac aatgaccag acctctagct ctcagggagg ccttggcggc ctaagtctga 180
ccacagagcc agtttcttcc aaccagagat acatcccttc ctcagaggct aacaggccaa 240
gccatctrct cagcactggg accccaggcg caggtgtccc cagcagtggg agagacggag 300
gcacaagcag agacacattt caaactgttc cccccaattc aaccaccatg agcctgagca 360
tgaggggaaga tgcgaccatc ctgcccagcc ccacgtcaga gactgtgctc actgtggctg 420
catttggtgt tatcagcttc attgtcatcc tgggtggtgt ggtgatcacc ctagttgggtg 480
tggtcagcct gaggttcaag tgcggaaga gcaaggagtc tgaagatccc cagaaacctg 540
ggagttcagg gctgtctgaa agctgctcca cagccaatgg agagaaagac agcatcacc 600
ttatctccat gaagaacatc aacatgaata atggcaaca aagtctctca gcagagaagg 660
ttctttaaaa gcaactttgg gtcccatga gtccaaggat gatgcagctg ccctgtgact 720
acaaggagga agagatggaa ttagtagagg caatgaacca catgtaaatt attttattgt 780
ttcatgtctg cttctagatc taaaggacac tagcattgcc ccagatctgg gagcaagcta 840
ccaacagggg agactcttct ctgtatggac agctgctgtg gaaatactgc ctgcttctcc 900
cacctctca gagccacagg aaagaggagg tgacagagag agagcaagga aagtgatgag 960
gtggattgat actttctact ttgcattaaa attattttct agcctgcaaa aaaaaaaaaa 1020
aaaaaaaaa aaaaactcga 1040
```

<210> 186

<211> 817

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (26)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (31)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (76)

<223> n equals a,t,g, or c

<400> 186

```
ancagctata gatcatgaca ggcaanggta nactgacagt acggtcggat tcccgggtcs 60
acccacgcgt ccgcangagc ggccgggtgg cgggaggaac cgttacggga actgaagttg 120
cggattaagc ctgatcaaga tgacaacctc ccaaaagcac cgagacttcg tggcagagcc 180
catgggggag aagccagtgg ggagcctggc tgggattggg gaagtcctgg gcaagaagct 240
ggaggaaagg ggttttgaca aggcctatgt tgtccttggc cagtttctgg tgctaaagaa 300
agatgaagac ctcttccggg aatggctgaa agacacttgt ggcgccaacg ccaagcagtc 360
ccgggactgc ttcggatgcc ttcgagagtg gtgcgacgcc ttcttgatgat gctctctggg 420
aagctctcaa tccccagccc tcatccagag tttgcagccg agtagggact cctcccctgt 480
cctctacgaa ggaaaagatt gctattgtcg tactcacctc cgacgtactc cggggtcttt 540
tgggagtttt ctcccctaac catttcaact ttttttggga ttctcgctct tgcatgcctc 600
ccccgtcctt tttcccttgc cagttccctg gtgacagtta ccagctttcc tgaatggatt 660
cccgccccca tccctcacc cccacctcac ttcaatccg ttgatacca ttggtcct 720
tttttggcag aacagtcact gtccttgtaa agtttttttag atcaataaag tcagtggctt 780
tcaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 817
```

<210> 187

<211> 1080

<212> DNA

<213> Homo sapiens

<400> 187

```
ctgccctgct gctggaacac cgagccagcc tgagcgctaa ggaccaagac ggctgggagc 60
gctgcacgcc gcggtacttg gggccaggtg cctggtggag ctgctcgtgg cgcacggggc 120
cgacctgaac gcaaagtccc tgatggacga gacgccccct gatgtgtgcg gggacgagga 180
ggtgcggggc aagctgctgg agctgaagca caagcacgac gccctcctgc gcgcccagag 240
ccgccagcgc tccttgctgc gccgccgcac ctccagcgcc ggcagccgcr ggaaggtggg 300
gaggcggttg agcctaacc agcgcaccga cctgtaccgc aagcagcacg cccaggaggc 360
catcgtgtgg caacagccgc cgcaccaccg cccggagccg cccgaggaca acgatgaccg 420
ccagacaggc gcagagctca ggccgcgcgc cccggargag gacaaccccg aagtggtcag 480
gccgcacaat ggccgagtag ggggtcctcc agtgcggcct ctatactcca agcgactaga 540
ccggagtgtc tcctaccagc tgagccccct ggacagcacc acccccaca ccctgggtcca 600
cgacaaggcc caccacacc tggtgacct gaagcgccag cgagctgctg ccaagctgca 660
gcgaccccca cctgagggggc ccgagagccc tgagacagct gagcctggcc tgcctgggtga 720
cacggtgacc cccagcctg actgtggctt cagggcaggc ggggacccac ccctgctcaa 780
gctcacagcc ccggcggtgg aggtccctgt ggagaggagg ccgtgctgcc tgctcatgtg 840
aggctgttgc tcagcatgca ggggccctgt cgcgggcaca gcccaggct gcctccccac 900
ggtgcgtgcc ctggtgctgc ggtgcagca cggaaacccc ggcttctact gtacaggaca 960
ctggccccctc tcagtcaga agacatgcct ggagggatgt ctggctgcaa agactatttt 1020
tatcctgcaa ctcttgataa agggctgttt tgccatggaa aaaaaaaaaa aaaaaaaaaa 1080
```

<210> 188

<211> 1286

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature  
<222> (1245)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1254)  
<223> n equals a,t,g, or c

<400> 188  
gcatgattct tgtttttag agatgcaggc tcaaaaagta atgcatgttt cttcagcaga 60  
actgaattat tcaactgccat atgactctaa acaccaaata cgtaatgcct ctaatgtaaa 120  
gcaccatgac tctagtgtc ttggtgtata ttcttacata ccttttagtg aaaatcctta 180  
tttttcacat tggcctccaa gtggtaccag ttctaagatg tctcttgatt tacctgagaa 240  
gcaagatgga actgtttttc ctctctctct gktgccaaaca tcctctacat ccctcttctc 300  
ttattacaat tcacatgatt ctttatcact gaattctcca accaatattt cctcactatt 360  
gaaccaggag tcagctgtac tagcaactgc tccaaggata gatgatgaaa tccccctcc 420  
acttcctgta cggacacctg aatcatttat tgtggttgag gaagctggag aattctcacc 480  
aaatgttccc aaatccttat cctcagctgt gaaggtaaaa attggaacat cactggaatg 540  
gggtggaaca tctgaaccaa agaaatttga tgactctgtg atacttagac caagcaagag 600  
tgtaaaactc cgaagtcta aatcagaact acatcaagat cgttcttctc cccacctcc 660  
tctcccagaa agaactctag agtcttctt tcttgccgat gaagattgta tgcaggccca 720  
atctatagaa acatattcta ctacttatcc tgacaccatg gaaaattcaa catcttcaa 780  
acagacactg aagactctg gaaaaagttt cacaaggagt aagagtttga aaattttgcg 840  
aaacatgaaa aagartatct gtaattcttg cccaccaaac aagcctgcag aatctgttca 900  
gtcaaataac tccagctcat ttctgaattt tggttttgca aaccgtttt caaaaccaa 960  
aggrccaagg aatccaccac caacttgga tatttaataa aactccagat ttataataat 1020  
atgggtgca agtacacctg caaataaaac tactagaata ctgctagtta aaataagtgc 1080  
tctatatgca taatatcaaa tatgaagata tgctaagtgt ttaatagctt ttaaaagaaa 1140  
agcaaaatgc caataagtgc cagttttgca ttttcataatc atttgcatg agttgaaaac 1200  
tgcaataaaa agtttgtcac ttgagcttat gtacagaatg ctatntgggg aacncttta 1260  
ggatgggttt tatttttcca tttttg 1286

<210> 189  
<211> 1738  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1480)  
<223> n equals a,t,g, or c

<400> 189  
gcggcgccct cggagccaaa ggcgcgcggc ggacacggcg gggccctcgc gcgcctggag 60  
acgatgccaa agctgcaggg cttcgagttc tggagccgca ccctgcgagg ggcccggcac 120  
gtcgtggccc ccatggtgga ccagagcgag ctggcctgga ggctgctgag ccggcgccac 180  
ggggcacagc tctgtacac gcccatgctg catgcccagg tctttgtccg cracgccaac 240  
taccggaagg agaactgta ctgcgaggtg tgcccaggg accggcccct catcgtgcag 300  
ttctgtgcca atgaccgga ggtgtttgtt caggcggtc tcctggctca ggattactgt 360  
gacgccattg acctgaactt gggctgcccc cagatgatag ccaagagagg tcactatggc 420

```

gcctttctgc aggacgagtg ggacctgctc caaagaatga ttttgctggc ccacgagaaa 480
ctctctgttc ctgtcacgtg caaaatccgt gtcttcccgg agattgacaa gaccgtgagt 540
acgcccagat gctggagaag gccggctgcc agttgctgac ggtgcacgga cgcaccaagg 600
agcagaaggg gcccctgtcg ggtgcagcgt cctgggagca tatcaaggct gtgcggaagg 660
ctgtggccat ccctgtgttt gctaaccgga acatccagt cctgcaggac gtggagcgct 720
gcctccggga cacgggtgtg cagggcgtca tgagcgcaga gggcaacctg cacaaccccg 780
ccctgttcga gggccggagc cctgccgtgt gggagctggc cgaggagtat ctggacatcg 840
tgccggagca cccctgcccc ctgtcctacg tccgggcccc cctcttcaag ctgtggcacc 900
acacgctgca ggtgcaccag gagctgcgag aggagctggc caaggtgaag accctggagg 960
gcatcgctgc tgtgagccag gagctgaagc tgccgtgtca ggaggagata tccaggcagg 1020
aggagcgaa gccaccggc gacttgccct tccactggat ctgccagccc tacatccggc 1080
cggggcccag ggaggggagc aaggagaagg cagggtgcgc cascaagcgg gccctggagg 1140
aaggaggagg tggcacggag gtcctgtcca agaacaagca aaagaagcag ctgaggaacc 1200
cccacaagac cttcgacccc tctctgaagc caaaatatgc aaagtgtgac cagtgtggaa 1260
acccaaaggg caacagatgt gtgttcagcc tgtgccgcgg ctgctgcaag aagcgagcct 1320
ccaaagagac tgcagactgc ccaggtcacg gattgctttt taaaaccaa ttggagaagt 1380
ctctggcctg gaaagaggcc cagcctgagc tgcaggagcc tcagccagca gcacctgga 1440
caccaggtgg cttctccgaa gtcatgggca gtgccctggn ctgaaggccc acaaccccca 1500
ccccaggac tgctgctgga gcctggacac gtccactta agaaaatgcc ttttactcag 1560
ggaatctcct gctacttaat gtgaaagac acgcccattg ccccttcgc cactctggg 1620
ggcctggaaa tgctgcagtg gggagcaggc ccaggctgg acctgccctg tcctcagcac 1680
gcgtgtgcaa aagtgaacaa taaatcattt caaagatgaa aaaamaaaaa aaaaaaaa 1738

```

<210> 190

<211> 1923

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1829)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1875)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1910)

<223> n equals a,t,g, or c

<400> 190

```

agcacatcaa atgccccac tccaagtacg ggtgcacgtt catcggaac caggacactt 60
acgagaccca cctggagact tgccgcttcg agggcctgaa ggagtttctg cagcagacgg 120
atgaccgctt ccacgagatg cacgtggctc tggcccagaa ggaccaggag atcgcccttc 180
tgcgctccat gctgggaaag ctctcggaga agatcgacca gctagagaag agcctggagc 240
tcaagtttga cgtcctggac gaaaaccaga gcaagctcag cgaggacctc atggagttcc 300
ggcgggacgc atccatgtta aatgacgagc tgtcccat caacgcgcgg ctgaacatgg 360
gcatcctagg ctccacgac cctcagcaga tcttcaagt caaagggacc tttgtgggcc 420

```

```

accagggccc tgtgtggtgt ctctgcgctt actccatggg tgacctgctc ttcagtggct 480
cctctgacaa gaccatcaag gtgtgggaca catgtaccac ctacaagtgt cagaagacac 540
tggagggcca tgatggcatc gtgctggctc tctgcatcca ggggtgcaaa ctctacagcg 600
gctctgcaga ctgcaccatc attgtgtggg acatccagaa cctgcagaag gtgaacacca 660
tccgggcccc tgacaacccg gtgtgcacgc tgggtctctc acacaacgtg ctcttcagcg 720
gctccctgaa ggccatcaag gtctgggaca tcgtgggcac tgagctgaag ttgaagaagg 780
agctcacagg cctcaaccac tgggtgcggg ccctggtggc tgcccagagc tacctgtaca 840
gcggctccta ccagacaatc aagatctggg acatccgaac ccttgactgc atccacgtcc 900
tgcagacgtc tgggtggcagc gtctactcca ttgctgtgac aaatcaccac attgtctgtg 960
gcacctacga gaacctcatc cacgtgtggg acattgagtc caaggagcag gtgcggaccc 1020
tcacgggcca cgtgggcacc gtgtatgccc tggcggtcat ctgcagcga gaccagacca 1080
aagtcttcag tgcatcctac gaccgggtccc tcagggtctg gagtatggac aacatgatct 1140
gcacgcagac cctgctgcgt caccagggca gtgtcacgc gctggctgtg tcccggggcc 1200
gactcttctc aggggtctgt gatagcactg tgaaggtttg gacttgctaa caggatccag 1260
ggcaggctgt ggtttccctc gaaccagccc tggaccttcc tgagccaggc tggccacatg 1320
gggtgggtctc ggggtttctg cctgccccgt gggcataggt ggacaggctc tggcagcccg 1380
gcagtgcctc ccccgctcca tgctcggcga gcctccctct actcggcact gtccctgtctg 1440
cccagccctc ctctgggtgc caggtaacgac gcttgccccg gcccaccctc catccccacc 1500
ctccatcccc accctagatg gagcgagggc ctttttactc accttttcta ccgttttttag 1560
actgtatgta gatttggtta cctcctggtt gaaataaatg ctccacagac tgtggctgtg 1620
agtggggaca gctcctcggg acaagggggc tgtgtgtggc cttgagggtg gtgtgcacag 1680
gcactggctg ctgtgagtgg gggggcatgg ggcagtttcc tttggtggac cccaggaytt 1740
cggsgccamtc cggggsctcc cctccctgct aggaggcaca ccctcagagg agctgcaagc 1800
ccgtggctgc ctgctacatg ccctgcttnc acgtggctgc acgctgacac acccacattc 1860
accaaaccga cccgngccct gggacgcaac cacgccagga ggaggacacn ggccgccgag 1920
agc 1923

```

<210> 191

<211> 250

<212> DNA

<213> Homo sapiens

<400> 191

```

ccaagtgtgt tgatacatta agctatgaga catctaaaat aatgaaactt ggaacttagt 60
ggaacatgta catgttttca gcatacttaa acccaaaaat cattaatttt cagaacttaa 120
tcagtgtctt tacatttgtt ttttctttta tgctagttag aaatggagga tgaaratata 180
attgrtgtgt tccaacagca gacgggrggt gtctactgaa aagggaacct gcttctttac 240
tccagaactc 250

```

<210> 192

<211> 1902

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (8)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (19)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (763)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1898)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1900)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1901)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1902)  
<223> n equals a,t,g, or c

<400> 192  
ngggacgntg gtagaccanc gcgtaccgct gagtcaratt ttggcatcaa cttgaagggc 60  
ccaaaaatca aaggaggtgc ggatgtttca gggggtgtca gtgcccara catcagcctt 120  
ggtgaagggc attttagtgt taaaggttcc gggggtgagt ggaagggacc ccaagtctcc 180  
tctgctctca acttgacac atctaagttt gctgggggcc ttcatttctc aggaaccaaag 240  
gtggaaggag gtgtgaaagg aggtcagatt ggactccagg ctcttgggct gagtgtgtct 300  
gggcctcaag gtcacttga aagtggatct ggaaaagtaa cattccctaa aatgaagatc 360  
cccaaattta ccttctctgg ccgtgagctg gttggcagag aaatgggggt ggatgttcac 420  
ttccctaaag cagaggccag catccaagct ggtgctggag acggcgagtg ggaagagtct 480  
gaagtcaaac tgaaaaagtc caagatcaaa atgcccaagt ttaatttttc caaacctaaa 540  
gggaaaggtg gtgtcactgg ctcaccagaa gcatcaattt ctgggtccaa aggtgacctg 600  
aaaagttcaa aggccagcct gggctctctg gaaggagagg cagaggccga agcctcttca 660  
ccgaaaggca aattctcctt atttaaaagt aagaagccac ggcaccgctg caaatcatt 720  
cagtgatgaa agagagttct ctggaccttc caccgccagc ggnacgctgg agtttgaagg 780  
tggggaagtg tctctggaag gtgggaaagt taaagggaaa cacgggaagc tgaaattcgg 840  
tacctttggt ggattgggt caaagagcaa aggtcattat gaggtgactg ggagcgatga 900  
tgagacaggc aagttacagg ggagtgggt gtccctggcc tctaagaagt cccgactgtc 960  
ctcctcttct agcaatgaca gtgggaataa ggttggcatc cagcttcccg aggtggagct 1020

```

gtcagtttcc acaaagaaag agtagcaggc ctttgtatgt gtgtacatat atatatatat 1080
aacaaaaacat cagccttggg tgggtgtgttc ctatataaac tccaaaggga aacacaccga 1140
ctgcctcagc aatcatgcaa agaccttgcc tggcccgggtg gcaagcgctg aaaaaccgac 1200
cgccctgtagg ctccctggaac tatacagata ggtaaagagt tccaagttcg tccagcccat 1260
gtgcaaagtc aacagtatct gccttaagat ttcatatata tatatttttt tgcattgact 1320
gctgagagct cctgtttact aagcaagctt ttgtgtttat tatcctcatt ttactgaac 1380
attgttagtt ttggggtaat ggaaaccac tttttcattg taatgacttt gggggctttt 1440
gttagtaagg gtgggtgggg tgatgggtg cagacggagg tcagggtctc ctctttcctg 1500
agactggatc tgttcaaaca gcaaacgccc acagatggcc cagagggtgt ggtagtcagg 1560
gtgtgtgggt gtttttaggg ttcttttagtg ttgtttcttt caccagggg tgggtgtccc 1620
agccagtttg gtgctgacgg tgagaggaaa ttagaatctg tttgcaaatt gtccaacca 1680
ccccctcaac atgaggggct tccattttct gtgttttgta agggaactgt ttccttcatg 1740
ccgccatgtt cctgatatta gttctgattt ctttttaaca aatgttatca tgattaagaa 1800
aatttccagc actttaatgg ccaattaact gagaatgtaa gaaaattgaw gctgtacaag 1860
gcaaataaag ckgttattaa cctgaaaaaa aaaaaanan nn 1902

```

<210> 193

<211> 560

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (20)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (528)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (535)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (559)

<223> n equals a,t,g, or c

<400> 193

```

ttttgcttaa agctatttan gtgacactat agaagggtacg cctgcaggta ccggtccgga 60
attcccggtt cgacccacgc gtccgggggt gcagacggag gtcagggtctt cctctttcct 120
gagactggat ctgttcaaac agcaaacgcc cacagatggc ccagagggtg tggtagtcag 180
ggtgtgtggg tgtttttagg gttctttagt gttgtttctt tcaccaggg gtggtgtgcc 240
cagccagttt ggtgctgacg gtgagaggaa attagaatct gtttgcaaat tgtccaaccc 300
acccctcaa catgaggggc ttccattttc tgtgttttgt aagggaactg tttccttcat 360
gccgccatgt tcctgatatt agttctgatt tctttttaac aaatgttatc atgattaaga 420
aaatttccag cactttaatg gccaatgaac tgagaatgta agaaaattga tgctgtacaa 480
ggcaataaaa gctgtttatt aaccttgaaa aaaaaaaaa aaagggnggg cccgncccat 540

```



tgccctaggg ggggttaant

560

<210> 194

<211> 590

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (589)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (590)

<223> n equals a,t,g, or c

<400> 194

ctgcaggtac cgggtccggaa ttccgggtcg cccacgcgtc aggcggcggc gatgaccttc 60  
tgccggctgc tgaaccggtg tggcgaggcg gcgcggagcc tgccctggg cgccaggtgt 120  
ttcggggtgc ggggtctcgc gaccggggag aagggtcacgc aactggcca ggtttatgat 180  
gataaagact acaggagaat tcggtttgta ggtcgtcaga aagaggtgaa tgaaaacttt 240  
gccattgatt tgatagcaga gcagcccgtg agcgaggtgg agactcgggt gatagcgtgc 300  
gatggcggcg ggggagctct tggccacca aaagtgtata taaacttggg caaagaaaca 360  
aaaaccggca catgcggtta ctgtgggtc cagttcagac agcaccacca ctagagcgtg 420  
tggcacgccg ggggtcccgc agcatcctgt gagcatttcc gcggggaagc tgagcacgtg 480  
aagctcgtcg gttctgtgcg aagggtattc ctggtgctga ataaagggtg ttgctgtcaa 540  
gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaann 590

<210> 195

<211> 691

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (10)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (579)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (618)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (639)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (657)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (672)

<223> n equals a,t,g, or c

<400> 195

```
attggcatcn tctgaaagcg ttttagacag gcagaatctc tggctctccc tctctgcatt 60
ccccaccag tgaatgaatg agaactctgca tttcttgaga tcataagaat actgacatac 120
agatgagata aaactcatgt gaatatcagt ttttaaggctg gtgggttcatt tgttttggtc 180
atattgagtc aggattgact aatgaactgt agaggttttg cattatgcaa atgctcttaa 240
tttcttgat taggaattag acgctcccc ccaagtctta aataatgttt taatctgtat 300
ccttttatta taagaagatt agtaatatc tacagataat aacaacaact ggtatagtat 360
attttattta cattcttcat tcttaaggaga aaatgctgag aagcttctgc agttcaagcg 420
ttggttctgg tcaatagtag agaagatgag catgacagaa cgacaagatc ttgkttactt 480
ttggacwtca agcccatcac tgccagccag tgaagaagga ttccagccta tgccctcaat 540
cacaatawga ccaccagatg accmacatct tcctactgna aaatacttgc atttcttggg 600
ctttaccttc cactctntt cctttaaaca ggattcttna aaccggaaat tgggtanctc 660
gccatttagg anccaaaaat tttgggtttt g 691
```

<210> 196

<211> 1772

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1749)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1769)

<223> n equals a,t,g, or c

<400> 196

```
gnataatgct ggccattttg cctttctgac atttccttgg gaatctgcaa gaacctcccc 60
tttcccttcc cmcaataaga ccatttaagt gtgtgytaaa caactacrga atactaaata 120
aaaagtttgg ccaaaaccaa ccatgaagct gcaaaggtgc ttgctcttac tstttcaaat 180
```

```

ttttgcaact ctartgtctc actttttaag gaacagcttg attgcaaagg agaaaataga 240
taagcaatga akttatctcc aacttcctaa aggccttatga cttctaaaaa gtgaatctat 300
cagcattcca catcagattt aaagcatcaa atgcctgtga aacagcaaaag atggttgaag 360
attgtgctca ttatgtttgt ggagtgtgta ttgattcaca gtagataacg ctggcagtaa 420
gagaaatcaa atgctaagag ttgttgaagc agaaggcggc tgattgttgg taagtcagtg 480
cagttgcata agcagtgtcg tcagaattgg tttggtgcag gcaatagatt ttgccttcaa 540
gggttcctgt ggatctcagg aaggcatcag tgttgattaa cactcataac tagggagtga 600
stggtagtta cttaagtaat tgaccaaag gaaaagggga agtaattaag gaaattggta 660
agtggaggta gtcaggargt tctygtggtt cttacayag attttacagc tttggstttc 720
attttgttta gctaaagtca tggggacaac tcttcaattt agaacttaag ttgaattata 780
aaaatgatgg atataagtgg tagctgtatc tagtgaagtg tctgtcagta agtgaacat 840
tttttggtgg tggcttatcc acaaacagtt tagttgtaga ataaaactta tgagtgcacat 900
ctggaaagta accatgctaa gatggcaagc acactggaaa caattaggcc acttggtctt 960
cttttgctgt attgttttat aagcctactt tacctcccag tcttgaaaac aagttttagt 1020
tttttattgg tttggagact agagccaata gtataatgtt ctcaaaggaa acagacttga 1080
gttgttggtg tagaggaact aacccaactt atatgatttt ttttttgttt ttgtcgtgta 1140
gttatggcac tgtcttattt ggaacatttg caactaggga taatacaaca tttttaactc 1200
tcatttgaca acctactact aatcacagac cacaagggtg atgaccaa attatgtggtt 1260
tttgcactcc atagttgtct tagcccaatc ttctatact cttacgatta cttgggttaa 1320
cgcytctgtg aggaccttct ggctcttgag ataccctaaa tatttaagat atttagatat 1380
cttgaagata gtataggata tagagattgt accaaatagg aatataagga gtatgttaaa 1440
atgaccagat acctgtttga tagtttactg acctagcaga tgtgtggaaa aggaatcaga 1500
tcttgattct tctgggttta tactgggtgt aaaacagaat gatacagaaa atgttttcct 1560
tgtttaactg gtagttgaac atagaacttg ggtattatag atcacttttc actttttgga 1620
atgttttgta ttgaaactta ataaaacttt aacatggcaa aaaaaaaaaa aaaaaaaaaa 1680
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740
aaaaaagana aaaaaaaaaa ggggggccnc cc 1772

```

&lt;210&gt; 197

&lt;211&gt; 675

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (657)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (671)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 197

```

accacgcgt ccggacttcc tcttcgttaa gtcggccttc ccaacatggc gcagtctatt 60
aacatcacgg agctgaatct gccgcagcta gaaatgctca agaaccagct ggaccaggaa 120
gtggagtctt tgtccacgtc cattgtctcag ctcaaagtgg tacagaccaa gtatgtggaa 180
gccaaggact gctgaacgt gctgaacaag agcaacgagg ggaaagaatt actcgtccca 240
ctgacgagtt ctatgtatgt ccctgggaag ctgcatgatg tggaacacgt gctcatcgat 300
gtgggaactg ggtactatgt agagaagaca gctgaggatg ccaaggactt cttcaagagg 360
aagatagatt ttctaaccaa gcagatggag aaaatccaac cagctcttca ggagaagcac 420

```

```

gccatgaaac aggccgtcat ggaaatgat agtcagaaga ttcagcagct cacagccctg 480
ggggcagctc aggtactatgc taaggcctga gagtttttgc agaaatggg cagagggaca 540
ccctttgggc gtggcttcct ggtgatggga agggctctgt gttttaatgc caataaatgt 600
gccagctggg caraaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaccccnngg 660
gggggcccgg naccc                                     675

```

<210> 198

<211> 557

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (451)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (461)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (464)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (488)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (492)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (495)

<223> n equals a,t,g, or c

<400> 198

```

tttaggtgac acgtatagaa ggtgcctgc aggtaccggw ccggaattcc gggtcgaccc 60
acgcgtccgg gaacacaaga tgccgaaggg aagaaggcga aggggaagaa ggtggccccg 120
gcccccgccg tcgtgaagaa gcaggaggcc aagaagggtg tcaacccgct gttcgagaag 180
cggcccaaga acttcggcat cggtcaggac atccagccca agcgggacct gacgcgttc 240
gtcaagtggc cgcgtacat ccggtgcag cggcacgcgc gatcctctac aagcggctga 300
aggtgccgcc cgccatcaac cagttcacgc aggcgctgga ccgccagacg gccacgcagc 360
ttgcttgaag ctggcgcaac attaccggcc cgagacgaag caggagaaga agcagcggtt 420
gttgccccgg gcggagaaga aarcggccgg ncaaggggga ntnccgaac aagcggsgcc 480
cgttggtntc gnaancgggg ttgaaaacgg ttcaacaagt tggttggaga acaagaaggc 540

```

gccattgggtt cgttatt

557

<210> 199

<211> 2611

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2549)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2560)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2585)

<223> n equals a,t,g, or c

<400> 199

tcnccgggtcg acccacgcgt ccggcgagga gtaccttacc aacttggccc acatggacat 60  
cgacaaggac tggaggcccc gctgtacctc acccccagg gctggtcctt cttcctccag 120  
cgctactacc aagtgggtcca cgaaggggca gaactcaggc acctcgacac tcagggtccag 180  
cgctgtgagg acatcctgca gcagctgcag gccgtggtac cccagataga catggaaggg 240  
gatcgcaaca tctggatcgt gaagccagga gccaaagtccc gcggacgagg catcatgtgc 300  
atggaccacc tggaggagat gctgaagctg gtgaacggca accccgtggg gatgaaggac 360  
ggcaagtggg tgggtgcagaa gtatatgtag cgccccctcc tcactcttgg caccaagttt 420  
gacctcagac agtggttcct ggtaactgac tggaaccac ttaccgtgtg gttctaccgc 480  
gacagctata tccgcttttc cacgcagccc ttctccctga agaacctgga caactcagt 540  
cacctgtgca acaactccat ccagaagcac ctggagaact catgccatcg gcatccactg 600  
cttccgccag acaacatgtg gtctagccag aggttccagg cccacctgca ggagatgggt 660  
gccccaaatg cttgggtccac catcatcgtg cctggcatga aggatgctgt gatccacgca 720  
cttcagacct cccaggacac cgtgcaatgt cggaaggcca gctttgagct ctatggcgct 780  
gacttcgtgt tcggggagga cttccagccc tggctgattg agatcaacgc cagccccacg 840  
atggcaccct ccacagcagt cactgcccgg ctctgtgctg gcgtgcaagc tgacaccctg 900  
cgcggtgtca ttgaccggak gctggaccgc aactgtgaca caggagcctt tgagctcatc 960  
tataagcagc ctgctgtgga ggtgcctcaa tatgtgggca tccggctcct ggtagagggc 1020  
ttcaccatca agaagcccat ggcgatgtgt catcggcgga tgggggtccg ccagcagtcc 1080  
ctctgctgac ccagcgaggc tctggggaag gcaaggactc ggggacctt acccacaggt 1140  
cagcttctag gaaaggcact ggggccagga gcctggggca cagtgagaag ccagtctcca 1200  
ctgccaccac ttcagcccc ggaaagggga agaaagccga ggtatcagga agttaagga 1260  
agttgcccaa gggtgcacag ctcaagaagg gcacagctgg gatgcagacc cagcccgtca 1320  
ccacttcccc agcctccaca ccaaggccca gctgccttct ccccatgtac tccgacacca 1380

```

gggccaggtc ctcagacgac agcacagcaa gctggtgggc actaaggccc tgtcgaccac 1440
aggcaaggcc ttgaggactc taccacggc taaggctctc atttccctcc caccgaacct 1500
tgattttcaag gtggcaccca gcatcctgaa gccaagaaag gtgggcctcg acctgtgact 1560
cacacccagt ggacagtgtc gagcacgggg tcagggctgg agggcacagg cagagggcag 1620
ctcccaggct ggctggcacc ccaagggaag agctggtctc cctcagaagc cccttcctcc 1680
acagacttct gatcatctcc ctcttctccc ctcccttcac accgaggctc ctgctctcct 1740
gtgcctccga ggccccagc tgggaagtgc ttgttgctc tgccctttga agtcggaaca 1800
attcctagca cctgtcggaa ggtcaaggcc aaaggcaaat tcaaggccag actgtgacaa 1860
accaggggtc gaggcctgcc ccatgaagag gctgagcccc ctgaaacccc tgccccttgt 1920
tggtacattc cagaggcgca ggggcctggg ggatatgaag ctagggaagc ccctgcttcg 1980
attccccact gcccttgttc tggatccaac accaaataaa aagaaacaag tgaagtattt 2040
ggggcttgac tccattgtct tggaggktc aagagtggat ggggcgaggc cgtgtacccc 2100
aggggtccaca gcaagagcct gagggcatca gcagytctc cgtgcagmga ggcccagaat 2160
tcccacctaa ggacagacat ggggcttcct atttagggac tccccagca tctccgatcc 2220
aggggtgggg agcgtgacct tcactttaca gatgaagaaa ctgagtctga aagaggaggc 2280
atggcttacc caagatcacg tggcagttag tcgacgcagg gacatattgc cagaactgcc 2340
gagcactggg agcccccaa ccccagagaa caagccaagc tagcagaatg acacctaccg 2400
ggcataggaa cgttaatgcc atgagacaag ggaaggattk gcttgctaaa mctcagccct 2460
tytgcagaag gcatkgttct atcccttctt cagcaaaggg gcaaggctac taaaaatgaa 2520
catccataag ccacaaccac tggagaaant tttgcactgn ttagtgtagt tggttgaatg 2580
tgggnccccg gaaagagatg ttacttggac c 2611

```

<210> 200

<211> 2316

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2280)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2282)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2302)

<223> n equals a,t,g, or c

<400> 200

```

ggcacgagga aacatggagt cctgtaggca aggtcttacc tgaatcagga tgagggagtg 60
gtgggtccag gtggggctgc tggccgtgcc cctgcttgct gcgtacctgc acatcccacc 120
ccctcagctc tcccctgccc ttactcatg gaagtcttca ggcaagtttt tcaattacaa 180
gggactgcgt atcttctacc aagactctgt ggggtgtggt ggaagtccag agatagttgt 240
gcttttacac ggttttccaa catccagcta cgactggtac aagatttggg aaggtctgac 300
cttgaggttt catcgggtga ttgcccttga tttcttaggc tttggcttca gtgacaaacc 360
gagaccacat cactattcca tatttgagca ggccagcatc gtggaagcgc ttttgcgga 420
tctggggctc cagaaccgca ggatcaacct tctttctcat gactatggag atattgttg 480

```

```

tcaggagctt ctctacaggt acaagcagaa tcgatctggt cggcttacca taaagagtct 540
ctgtctgtca aatggaggtg tctttcctga gactcaccgt ccactccttc tccaaaagct 600
actcaaagat ggaggtgtgc tgtcaccat cctcacacga ctgatgaact tctttgtatt 660
ctctcgaggt ctaccccag tctttgggcc gtatactcgg cctctgaga gtgagctgtg 720
ggacatgtgg gcagggatcc gcaacaatga cgggaactta gtcattgaca gtctcttaca 780
gtacatcaat cagaggaaag agttcagaag gcgctgggtg ggagctcttg cctctgtaac 840
tatccccatt catTTTTatct atgggccatt ggatcctgta aatccctatc cagagttttt 900
ggagctgtac aggaaaaacgc tgccgcggtc cacagtgtcg attctggatg accacattag 960
ccactatcca cagctagagg atcccatggg cttcttgaat gcataatgg gcttcatcaa 1020
ctccttctga gctggaaaag gtagcttccc tgtattacct cccctactcc cttatstgtt 1080
gtgtattcca cttaggaaga aatgcccaga agaggtcctg gccatcaaac ataattctct 1140
cacaaagtcc actttactca aattggtgaa cagtgtatag gaagaagcca gcaggagctc 1200
tgactaaggt tgacataata gtccacctcc cattactttg atatctgac aaatgtatag 1260
acttggcttt gttttttgtg ctattaggaa attctgatga gcattactat tctactgatg 1320
agaaagacgt tcttttgcac aaaagacttt ttttaacact ttggacttct ctgaaatatt 1380
tagaagtgtc aatttctggc ccaccccaa caggaattct atagtaagga ggaggagaag 1440
gggggctcct tccctctcct cgaatgacgt tatgggcaca tgccttttaa agttcttta 1500
agcaaacacag agctgagtc tctttgtcat acctttggat ttagtgtttc atcagctgtt 1560
tttagttata aacattttgt taaaatagat attggtttaa atgatacagt attttaggta 1620
tgatttaaga ctatgattta cctatacatt atatatatt tataaagata ctaaaccagc 1680
atacccttac tctgccagag tagtgaagct aattaaacac gtttggtttc tgaataaatt 1740
gaactaaatc caaactattt cctaaaatca caggacatta aggaccaata gcactgtgc 1800
cagagatgta ctgttattag ctgggaagac caattctaac agcaaataac agtctgagac 1860
tcctcatacc tcagtgttta gaagcatgtc tctcttgagc tacagtagag ggggaaggat 1920
tgttgtgtag tcaagtcacc atgtgaatg tacactgatt cctttatgat gactgcttaa 1980
ctccccactg cctgtcccag agaggctttc caatgtagct cagtaattcc tgttacttta 2040
cagacaggaa agttccagaa actttaagaa caaactctga aagacctatg agcaaattgg 2100
gctgaatact ttttttttaa agccacattt cattgtctta gtcaaagcag gattattaag 2160
tgattattta aaattcgttt ttttaaatta gcaacttcaa gtataacaac tttgaaactg 2220
gaataagtggt ttattttcta ttaataaaaa tgaattgtga caaaaaaaaa aaaagggccn 2280
gncccgTTTT aaaagggatc cnaagcttta ccgtac 2316

```

<210> 201

<211> 1147

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (5)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (11)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (12)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (19)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1145)  
<223> n equals a,t,g, or c

<400> 201  
cgcannccac nnggtggang ccgctctaga atatggatcc cccgggactg cagggagtcc 60  
aaggtacagt cgcgcgctgc ggagcttggt actggttact tggcctcatg gcggtccgag 120  
cttcgttcga gaacaactgt gagatcggct gctttgcca gctcaccaac acctactgtc 180  
tggtagcgat cggaggctca gagaacttct acagtgtgtt cgagggcgag ctctccgata 240  
ccatccccgt ggtgcacgcg tctatcgccg gctgccgcat catcgggcgc atgtgtgttg 300  
ggaacaggca cggctctctg gtacccaaca ataccaccga ccaggagctg caacacattc 360  
gcaacagcct ccagacaca gtgcagatta ggcgggtgga ggagcggctc tcagccttg 420  
gcaatgtcac cacctgcaat gactacgtgg ccttggtcca ccagacttg gacagggaga 480  
cagaagaaat tctggcagat gtgctcaagg tggaagtctt cagacagaca gtggccgacc 540  
aggtgctagt aggaagctac tgtgtcttca gcaatcaggg agggctggtg catcccaaga 600  
cttcaattga agaccaggat gagctgtcct ctctcttca agtccccctt gtggcgggga 660  
ctgtgaaccg aggcagttag gtgattgctg ctgggatggt ggtgaatgac tgggtgtgct 720  
tctgtggcct ggacacaacc agcacagagc tgtcagtggg ggagagtgtc ttcaagctga 780  
atgaagccca gcctagcacc attgccacca gcatgcggga ttccctcatt gacagcctca 840  
cctgagtcac ctccaagtgt gttccatggg ctccctggctc tggactgttg ccaaccttct 900  
ccacattccg cccaatctgt accggatgct ggcagggagg tggcagagag ctactggga 960  
ctgaggggct gggcacccaa cccttttcca cctgtgctta tcgcctggat ctatcattac 1020  
tgcaaaaaacc tgctctgttg tgctggctgg caggccctgt ggctgctggc tgagggttct 1080  
gctgtcctgt gccaccccat taaagtgcag ttccctccgg aaaaaaaaaa aaaaaaagg 1140  
cggnac 1147

<210> 202  
<211> 688  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (477)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (684)



<223> n equals a,t,g, or c

<400> 202

```
acgtaccggt cccgtaattc cccgggtcgac ccacgcgtcc gctcggcggg cgctgttgag 60
ggagtcgggc' cgcgactgtg gtcgttttta taccttcccg cgcggacgcc ggcgctgcc 120
acggaagggc gggtaggacg gagtttcgtc atgttgacca ggcccatttg agatctttga 180
agatatactc aacgtgaggc tctgctgcc aagaagtga gattaagtgc tggaaaggcg 240
tggccacttg gctctgggtg gccaacgatg agaactgtgg catctgcagg atggcattta 300
acggatgctg ccctgactgc aagggtcccc gcgacgactg cccgctggtg tggggccagt 360
gctcccactg cttccacatg cattgcatcc tcaagtggct gcacgcacag cagggtgcagc 420
agcactgccc catgtgccgc caggaatgga agttcaagga gtgaggcccg acctggntct 480
cgctggaggg gcacctctgag actccttccat catgctggcg ccgatggctg ctggggacag 540
cgcccctgag ctgcaacaag gtggaacaaa gggctggagc tgcgtttgtt ttgccatcac 600
tatgttgaca cttttatcca ataatgaaa actcattaaa ctactcaaat cttaaaaaaa 660
aaawaaawaa atctcggggg gggncccg 688
```

<210> 203

<211> 304

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (269)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (287)

<223> n equals a,t,g, or c

<400> 203

```
aaatgtgaaa actaaggcct tgcaagccta tgggtcaccc aggggtagga tcaggcacct 60
taactctaga gcccatcttc ctaaccactg agccatgatt gtcttacaat tttgaatact 120
gcaaaactgg aagaattgtc tggtatttat ctaagctgtt cataagctgg aacaagtaga 180
tctgagggtg agaggagttc tgttttaact aggactgagt ttcaaataga gatgtttcag 240
actatagagg gggaaaaatg gcckgggang tccataaatc taagccngtt tcatggatgt 300
tttt 304
```

<210> 204

<211> 417

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (380)

<223> n equals a,t,g, or c

<400> 204

```
gggtcgaccc acgcgtccgc gcgggcgggg acggagctcg gcgtgcttgc tgctggaggg 60
```

```

tgatggccct gcaaggctgt gggctccgac ctcaccggga gtcgamarcg agaggttcgc 120
cgaagagcga ggttctgggc gagcgctgaa cgccggcccc aagcaccggt ggtctttaca 180
cagtcgcgct ccacagactc tgacgaagac gtggatctgc tctcgcttta gctgctcgcg 240
gtcctccaga tcatgtccgc gactcctgcg actccgcgcg gaaaaaaaaaag tttgccaggc 300
gtggactcaa tgacytttcc aastgtgcgc ctcgytgcct ggaccgggtt gagcgcggtt 360
gccaagttg aactttttgn ggggagggtt ttctctaagg gctgtgtct caatggg 417

```

<210> 205

<211> 551

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (450)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (458)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (471)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (484)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (519)

<223> n equals a,t,g, or c

<400> 205

```

gggtcgaccc acgcgtccga ctagttctag atcgcgagcg gcccgccctt tttttttttt 60
tttttttttt tggtttccag agtttggtt tattttgcag tacagaaatc atctggagcc 120
gtctgagaca gacatccctg aagcggaggc tctgtcaaata caatactgcg tcgcacttrg 180
tccgttgagg aagccacacc tggggtacaa aagaagcttc tacgtttacc cgctgtacca 240
cggatttctt tcccctttgc tcttaccat tttaccagg gaaaacaccg cacagaggct 300
tccctcgga tgacgctcgg gtctggagtt gggttagaat tgtgggcccg cgtgaccccc 360
acctgtggct gtgttccgtg gccctgtcct aaacagctga cgggacacag acgtagaggg 420
gcggggccac gcagggatgc tgttcccaan tcacgganta tctgggtggc ntcgcaatgg 480
ccantgggac agatggcacg tgaaaggggc cgttccggnt ctcaagcggc agaagcacia 540
gaccgcggag g                                     551

```

<210> 206

<211> 1101

<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (21)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (479)  
<223> n equals a,t,g, or c

<400> 206  
tccccgggtcg acccacgcgt nccgcccgt ggaggctgga gcttccgggc cctggaaagg 60  
ggtccccgcg cgcgccgggt cggaggcaga ccctggggtt tgggggacat gggcatttgg 120  
ggcgctgaa cccaagacct ctggatgagc tgccccgttc agaccatgga tcctgaggtg 180  
accttgctgc tgcagtgcc tggcgggggc ctgccccagg agcagataca ggccgagctg 240  
agccccgcc atgaccgtcg cccactgcca ggtggggacg aggccatcac tgccatctg 300  
gagaccggc taaaggcca accctggctc ttcgacgcc ccaagttccg cctgcaactca 360  
gccaccctgg cgcctattgg ctctcggggg ccacagctgc tctgcccct gggccttact 420  
tcctaccgag acttcctggg caccaactgg tccagctcag ctgcctggct gcgacasang 480  
ggtgccaccg actgggggtga cagcaggcc tatctggcg acccactggg ggtggcgct 540  
gcactagcca cagccgatga cttccttgy ttctgccc gctccccgca ggtggctgag 600  
gccctgggc tgggtggacgt acctggtgg caccctgagc ctcaggccct gtgcccctgg 660  
ggcagcccc agcaccagga cctcgtggg cagctggtg tacatgaact cttttccagt 720  
gtccttcagg agatctgtga tgagtgaaac ctgcccgtgc tcaccctgag ccagcccctg 780  
ctgttkggca tcgcccgaaa tgagaccagt gctggccgag ccagtgccga gttctatgtc 840  
cagtgcagcc tgacttctga gcaggtgagg aagcactacc tgagtggggg acccgaggcc 900  
cacgagtcta caggaatctt ctttgtggag acacagaacg tgcggagatt gcccgagacg 960  
gagatgtggg ctgaactctg cccctcgcca aaggcgccat catcctctac aaccggggtc 1020  
agggaagtcc cactggagcg gccctagggt ccccgccct actcccgccg ctctgaaaat 1080  
aataaacgac tttattcttg g 1101

<210> 207  
<211> 515  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (428)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (439)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (449)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (456)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (474)  
<223> n equals a,t,g, or c

<400> 207  
gggtcgaccc acgcgtccgc ccacgcgtcc ggcrgataga gcgccatgaa ggcctcgggc 60  
acactgcgag aatacaaggt ggtggggcgc tgcctgccc ccccaaatg tcgcactccg 120  
ccgctgtatc gcatgcgaat ctttgaccct aatcacgtgg tcgccaaagtc ccgcttttgg 180  
tactttgtgt ctcagctgaa aaagatgaag aagtcctcag gggaaatcgt ctactgtgga 240  
cagggtgtttg agaaatcccc cttgcgagtg aagaacttcg gcatctggct gcgctatgac 300  
tcgagaagcg gtaccacaaa catgtaccgg ggagtaccgg ggacctgacc amcgcgggcg 360  
ccgtcaccca gtggttaccg agacatgggc gcccgacacc gttgcccag cgcattcgat 420  
tccagatnct tgaagtggna ggagattgnc agccancaat tgccgccggg ccancattca 480  
agcatttcca aggattccaa gatcaattcc cattg 515

<210> 208  
<211> 269  
<212> DNA  
<213> Homo sapiens

<400> 208  
aagcattgtg ggtaaaggcc tggaggcagg aaagtgaagg acaatttcaa gaaactcagt 60  
tcatcaattt tcatcaaacac cttcctgggc catgcctggg tactgagraa cccagccctg 120  
aatctggaca tcattttccc tttcagagca tagaatgcag ggggatccag ggaatgggtt 180  
aacagaagag gaagctggwt caaggagacc tttgcgtacc aggtgaaggt gtttgaactt 240  
tgttcttgca ggcaggcaga gcacggaca 269

<210> 209  
<211> 734  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (278)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (732)  
<223> n equals a,t,g, or c

&lt;400&gt; 209

```
cgactggttg ttaccgagga agatggcggc gccagaccgc aggcgctagg gaagatcgca 60
ccgcggacgc ccgctgagct tggcgcacgg gccgaccagg agctggtgac tgccctcatg 120
tgtgatttgc ggcggccagc ggcagggtgg atgatggact tggcctacgt ctgtgagtgg 180
gagaaatggt ccaagagcac ccaactgccc tcggtgcccc tggcctgcgc ctggtcctgc 240
cgaaatctca tcgccttcac catggacctg cgcacgantg accaggacct gacccgcatg 300
atccacatcc tggacacgga gcacccctgg gacctgcact cgatcccctc agagcaccac 360
gaggccatca cctgcctgga gtgggaccag tcaggctccc ggctcctgtc agcagatgcc 420
gacgggcaga tcaagtgtg gagcatggcg gaccacctgg ctaatagctg ggagagctca 480
gtgggcagcc tagtggaggg ggacccatt gtggccctgt cctggctgca caatggtgtg 540
aaactggccc tgcacgtgga gaagtcgggc gcctccagct tcggggagaa gttctccga 600
gtcaagttct caccygttct cacgctgttc ggcggcaagc catggagggc tggatcgcg 660
tgacggtcag cggcctggtc accgtgtccc tgctgwaasc agcgggcagg tgctgacgtc 720
caccgagagc tntt 734
```

&lt;210&gt; 210

&lt;211&gt; 658

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (561)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (567)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (577)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (580)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (636)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (654)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 210

```

ccccgccagcg ttgagggttta tcacgacagc ctgtgccgaa aaatctggcg tgaggatgat 60
aaatggcatg tcattttttcg tgcagacggc tgggagcaac atattaccgc ccgctatctg 120
gtcgggtgccg atggcgcaaaa ctgatgggtg cggcgacatc tctaccggga tcatcaaadc 180
cgtaaatatg tcgctatcca gcagtgggtc gcggagaaac atccgggtgcc gttctactcc 240
tgcattctttg ataattcgat aactaactgt tattcatgga gtatcagcaa agacggktat 300
tttatctttg gcggtgccta tccaatggaa agacggtcag acgsgtttca sgacgcttra 360
agagaaaatg agcgcccttc agttccagtt tggtaagacg gtgaaaagcg aaaaatgcac 420
gggtgctgtt tccctcgcg cggcaggatt ttgtctgcgg taaggacaac gcctttcttg 480
attggtgaac ggcgggattt atcagcgcca gctcgctgga agggattagc tatgcgctgg 540
atagcacaga catttctgcg ntcgtgntac tgaacanccn gagaagctca atacggttac 600
tggcgcgcca cccgaaactg ggttaaactc ttcggnaaga tataaaaagc catnctga 658

```

<210> 211

<211> 204

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (91)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (94)

<223> n equals a,t,g, or c

<400> 211

```

attcggagag ccatctctga cagttagagc cgatatcact ggaagatatt caatcgtctc 60
tatgcttacg acctgcagat acagtctgtt nttncacatg aagaaagtct caagttgctg 120
aagactgaat tgtaagaaaa atctccagcc cttctgtctg cagcttgaga cttgaaccag 180
agagtgtgag agctgctgtt ggag 204

```

<210> 212

<211> 1271

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1222)

<223> n equals a,t,g, or c

<400> 212

```

ttccgcagcc ttgccccagc ccactcccc tctcacccta ccacagagca tggtaaatac 60
caagcccagag aagacggagg aggactcaga ggaggtgagg gagcagaaac acaagacctt 120
cgtggaaaaa tacgagaaac agatcaagca ctttggcatg cttcgccgct gggatgacag 180
ccaaaagtac ctgtcagaca acgtccacct ggtgtgcgag gagacagcca attacctggg 240
catttgggtgc attgacctag aggtggagga gaaatgtgca ctcatggagc aggtggccca 300
ccagacaatc gtcatgcaat ttatcctgga gctggccaag agcctaaagg tggacccccg 360
ggcctgcttc cggcagttct tactaaagat taagacagcc gatcgccagt acatggaggg 420

```

```

cttcaacgac gagctggaag ccttcaagga gcgtgtgcgg ggccgtgcca agctgcgcat 480
cgagaaggcc atgaaggagt acgaggagga ggagcgcaag aagcggctcg gcccggcg 540
cctggacccc gtcgaggtct acgagtcctt ccctgaggaa ctccagaagt gcttcgatgt 600
gaaggacgtg cagatgctgc aggacgcat cagcaagatg gacccaccg acgcaaagta 660
ccacatgcag cgctgcattg actctggcct ctgggtcccc aactctaagg ccagcgaggc 720
caaggaggga gaggaggcag gtcctgggga ccctacttg gaagctgttc ccaagacggg 780
cgatgagaag gatgtcagtg tgtgacctgc ccagctacc accgccacct gcttcaggc 840
ccctatgtgc cccttttcag aaaacagata gatgccatct cgcccgctcc tgacttcctc 900
tacttgcgct gtcgagccca gcctgggggg ccgcccagc cctccctggc ctctccactg 960
tctccactct ccagcgccca ttcaagtctc tgctttgagt caaggggctt cactgcctgc 1020
agcccccat cagcattatg ccaaaggccc ggggggtccg ggaagggcag aggtcaccag 1080
gctggtctac cagtagttg gggaggggtcc ccagccaagg ggccggctct cgtcactggg 1140
ctctgttttc actgttcgtc tgctgtctgt gtcttctatt tggcaaacag caatgatctt 1200
ccaataaaaag atttcagatg cnaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaacaaaaa 1260
aaaaaaaaaa g 1271

```

<210> 213

<211> 1025

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (991)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1007)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1019)

<223> n equals a,t,g, or c

<400> 213

```

cggacgcgtg ggcgagcgtg atagccaaca ggaaccggga gcgggggtccc gggactggga 60
agaaaacggcg gccgggaggg ggctccgggg accatggggc tcctgacctat tctgaagaag 120
atgaagcaga aagagcgagg gctgcgactg ctcatgcttg gcctggacaa tgctggaaag 180
acaacccatcc tgaagaagtt caatggggag gacatcgaca ccatctcccc aacgctgggc 240
ttcaacatca agaccctgga gcaccgagga ttcaagctga acatctggga tgtgggtggc 300
cagaagtccc tgccgtccta ctggcggaac tactttgaga gcaccgatgg cctcatctgg 360
gtagtggaca gcgcagaccg ccagcgcatg caggactgcc agcgggagct ccagagcctg 420
ctggtggagg agcgcctggc cggagcaacc ctccctcatct ttgctaataa gcaggacctg 480
cctggagcac tgtcctctaa cgccatccgc gaggycctgg agctggactc catccgcagc 540
caccactggg gcatccaggg ctgcagcgcc gtcaccgggg agaacctgct gccgggcatac 600
gactggctcc tggatgacat ttccagccgc attttcacag ctgactgaac cactccagat 660
gccccccacc tagcagtcca ggtccctcaa ccttcaccaa acactacca tgggggggtt 720
ggagtcagcc ggccaaacta acactcccc tcctccaccc cagcctgctg ctgctactgc 780
tgcccgctgc tgctctgtgg ccaccgggt cccatggcgg gagggtctgt ccctggctgt 840

```

```

ctctctggct cctgacctgg cctttggcta ccataccaag aagagagggc tgggcgggga 900
ggagctgcta ctgctgctac cgaggtgtg ggccatcc ttcactcagt tgtgaaataa 960
accgctcctt gccccgmaaa aaaaaaaaaa naaaaaaaaa aaaaaanccc ggggggggnc 1020
ccgga 1025

```

```

<210> 214
<211> 351
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (332)
<223> n equals a,t,g, or c

```

```

<400> 214
ggcacgagtr aactatatac ctcaaagaat tagaaaaaga agaacaaact aagctcaaag 60
ttagcagaag gaagaaata gtaaatatta cagcagaagt aaagtagagg ctagaaaaat 120
aataaaaaag atcaacaaaa tggatattgt tctcatacta tgataaagac atacttgaga 180
accgcattat ttatggggaa aagaagttaa attgactcac agttccacag gctgtacagg 240
aggcatggct tagggaggcc tcagggaaac ttagratcca tgggtggaagg tgkargagga 300
agcatgcacc atcttctactg gccagagcag gnggagagag agcaaatttg g 351

```

```

<210> 215
<211> 1087
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (1075)
<223> n equals a,t,g, or c

```

```

<400> 215
gctggagtcc cagtccaccc gccacgcccc agcagggcct gtccgccttc tacctctcct 60
actttgacat gctgtaccct gaggacagca gctgggcagc caaggccctt ggggccagca 120
gtcgggagga gccacctgag gagcctgagc agtgcccgtt cattgacagc caagccccag 180
cgggcagcct ggacttggtg cccggcgggc tgaccttga ggagcactcg ctggagcagg 240
tgcagtccat ggtggtgggc gaagtgtca aggacatcga gacggcctgc aagctgtctca 300
acatcaccgc agatcccatg gactggagcc ccagcaatgt gcagaagtgg ctctgttga 360
cagagcacca ataccggctg ccccccatgg gcaaggcctt ccaggagctg gcgggcaagg 420
agctgtgctg catgtcggag gagcagttcc gccagcgtc gccctgggt ggggatgtgc 480
tgcacgccc cctggacatc tggaaagtcag cggcctggat gaaagagcgg acttcacctg 540
gggcgattca ctactgtgcc tcgaccagtg aggagagctg gaccgacagc gaggtggact 600
catcatgctc cgggcagccc atccacctgt ggcagttcct caaggagttg ctactcaagc 660
cccacagcta tggccgcttc attaggtggc tcaacaagga gaagggcctc ttcaaaattg 720
aggactcagc ccagggtggc cggtgtgtrg gcattccgca gaaccgtccc gccatgaact 780
acgacaagct gagccgctcc atccgscagt attacaagaa gggcatcatc cggaagccag 840
acatctycca gcgsetcgtc taccagttcg tgcacccat ctgagtgcct ggcccagggc 900
ctgaaacccg ccctcagggg cctctctcct gcctgccctg cctcagccag gccctgagat 960
gggggaaaaac ggcagctctgc tctgtctgtc tgaccttcag agcccaaggc caaggagggg 1020

```



caaccaactg cccaggggga tatgggtcct cttggggcct tcgggaccct ggggncaagg 1080  
ggctttc 1087

<210> 216

<211> 1977

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (8)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (11)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1873)

<223> n equals a,t,g, or c

<400> 216

cgctgcnng nacgggtccg gaattcccgg gtcgaccac gcgtccggca gaagaagagg 60  
aggaggaaga tgaggaagag gaggaagaag aggaggagga ggaggaagaa ggcctcagc 120  
agcgagggca gggagagaag tcagccacgc cctcacggaa gattctggac cctaactg 180  
gggagccagc tccctgctg tctctccac ctctgcaga cgtctccacc ttcctggtt 240  
ttccctctcc agagaagctg ctgcgcctag ggcccaagag ctccgtgctg atagccagc 300  
agactgacac gtctgacccc gagaagggtg tctctgcctt cctaaagggtg tcatctgtgt 360  
tcaaggacga agctactgtg aggatggcag tgcaggatgc agtagatgcc ctgatgcaga 420  
aggctttcaa ctctctgtcc ttcaactcca acaccttctt caccaggctc ctctgacaca 480  
tgggtctgct caagagtga gacaaggta aggccattgc caacctgtac ggccccctga 540  
tggcgtgaa ccacatggtg cagcaggact atttcccaa ggcccttgca cccctgctgc 600  
tggcgttcgt gaccaagccc aacagcgccc tggaaacctg ctcttcgcc cgccacagtc 660  
tgctgcagac gctgtacaag gtctagactc aaagcctctc ccatcccttg gcctggacca 720  
gtgagctggg gagggactcg gatgaactga ggcgcagcct acgccattgc cttggacagg 780  
actctggcca caggcagggc gggctctgtgt cccatgtgtc ctgtcagtc cctgagtatg 840  
tgtgtgggtg tggcgcatgt gcaggctctgt gcctcctgtc gggatttggg ttttaacgtc 900  
ttctgctggc ccagccctgc tctgttgttg ggagttggcc cccaggggaa agggctgtga 960  
gctgctccgc cattaaactc acctccacct gagggcgctc tgctgatctc cgcttggg 1020  
ctgatggccg tccccacca cctgccttcc ggcccggtc cctggcgag caraaccar 1080  
ggagttgccc gcgtgctgtc cttccctct gtgttgtgat tgggttgtt cctgccctgc 1140  
ctggggctgc ttctcgtcac caagccctgg tctgcggca gctgtcacc ctaccatcca 1200  
taccactgtg ctgaccgctc agcctgaaga gcagagaatg ccatgggtgg gactgtggg 1260  
gtcggatcgt ggggttgttg gcagagggca accctgggcc ccacaccgtg tggacaggca 1320  
gacaccagat tgtccaggag caggagctgc tgggactgc ctggccccgg acctagtgg 1380  
ccttctcctg gctgctgaga tgtcgtctgt gactggcctg gctggagggg gagtgttgac 1440  
aaccctaaagc tggtctccag tctggggagg gagaggcagg gtccccaatg tccgagctgc 1500  
atctggagc tgctcttaaa ggacctcctg gggcagggga gcggtagggt ctggactggg 1560  
cagatgctgt atgacctccc tgagcaccgc tgactgcccc atgctttccc ctttgtgtc 1620

```

tgtgtgtgtc tggctgtgcc cgggggcttc acaaataaag tcgtgtggca gcttcagaga 1680
ctcagaaact ctcactgaaa gcgggtagt ctcggggggcc gttgtacgtg gagtcccacc 1740
tcggcagagc atgcggcccc gcagcagtct gtggggcagt cagccctgca gaaggggccc 1800
gcctcggcct caggcactac ctgggaagtg gcagtcctga gtggggggccc attttcctgc 1860
ctggscacac ctnaccacgc accctgcctt tgggctgcag ctcgcttggc ttctgcgttg 1920
ctccttcact atggaagcca cctcccttgg gatcctttgc tccactgcca catatgt 1977

```

<210> 217

<211> 2815

<212> DNA

<213> Homo sapiens

<400> 217

```

aattcccggg tgcacccacg cgtccggggcg cccgcgtctg agcccagagg gctgtggagt 60
gtcccggccg gccccgagca ccccgcgct gtccgtcccc cgctccggtc ttccgctttg 120
gcttccaact agttaaatgc ccttgagcgc gggtttccgc ggcccggctc ttccgccccg 180
cggcgcgagt tgagccgttt cccgcgctg tccgcgcggg cgctccgaca gcggctctgc 240
agggtccgcg gccacgcgtc ggccaccgct cggccgccac tcaaggctca cgcgtcgatg 300
tgtagctaca tagttatctg tgtacatcca cgctggggca tttttctcct gcttaatgag 360
gacttgactc gggagcaagt gtgaatcatt gccggggctg ggaaaggagg aaggcgcatt 420
taacccccctc ccacccctct ccatgtccgt gtgtcactcg gctcgggtcca cctggcgcg 480
ccggctcctgg ggctgctgct gctgttgacg acgacgacga cgacgggggc tgctctgct 540
gtcccgggag tttcctcctg ctccggccac acagctcctg gggattgttc ctcttcgaac 600
cagaacctcg gcctgaccgg cactttggct ccaaaataac tttatttttg ggggagaaag 660
cacatcacga accagtcaaa atcgtgggtt atttctgtaa cgtgaagact tctgctctt 720
tttctttgtt tgtttttttc gtaaaccatct ggggtgtatat caaacggcaa gatgtccagt 780
aatgtcccgg cggatatgat aaatttgccg ctcatttttg taagcggaaa aacaaaagag 840
ttcctgtttt ctctaacga ttctgcttct gacattgcaa agcatgtata tgacaattgg 900
ccaatggact gggaagaaga gcaggtcagc agtccaaata ttctacgact tatttatcaa 960
ggacgatttc tacatggaaa tgtcacatta ggagcattaa aacttccttt tggcaaaaca 1020
acagtgatgc atttgggtggc cagagagaca ttaccagagc caaactctca aggtcagagg 1080
aatcgtgaga agactggaga gagtaattgt tgtgtaatcc tgtaaacact gtctgcctag 1140
tgtgatgtga tatagtcttt gtctttcatg ctgctgggac agaaaagacc cgacattgct 1200
tcagaaaaccg ttcagaacag tctgcctgta aacacatgga actgaattac cacatgaaca 1260
ctgtcatctt ttctcatgaa agtaaaaaga accaagaaca tttttcactc tgatttttta 1320
tttcttgat tttttgttga gctgttttaa cacatatttg tttttgaatg cagtcaatct 1380
ccaggggaaa agttaacaag ttatctttcg tagcagaaac cattttgctg ccacaaaatt 1440
ttcatcatca gaactaataa atcaagtgtt ccaaatacaa tttgcactaa aaagattggc 1500
attattttcc tcatcagcag aatttataac agtgtgtggt atctagaaat acttatatat 1560
acaattccac actggaagac actcagcaat taatgaagt aattactggg ccaacttgag 1620
aggaaaaaat ggaaaagaaa ctaaaatgtt ggggtgaattc taccaaagtc agccgtggtg 1680
gctgcactgg cacagaatac taaactgagt gtgactatct tcaactgcaac aaatgaaaaa 1740
acaaaatgtg cctgttttaa gcactcagta gagggctgat gaaactaatt ttttttcctt 1800
taagacatgc actcttgagt cctacagtaa ctgagtgttt gtttagacag cacaagaagg 1860
ggtagagtg cgtctcctag ccttaatgtg ggagggtagt ttcagtcact catcggttt 1920
cattatttg crgaaatatt agaaaacctc attgatcaat tttatgtatt tgaatatcag 1980
caaattgaaa ttttccataa ttatcattaa tttgtaacca catccagtgt catgcttact 2040
ccttagagtt cagatgaatt cttaaaatta aaaaaaact ccatagtact aattttgktt 2100
ttttatatag tttgcgtttg atattagtgc ttgcaattgt attaaagtca aaagctgatt 2160
tttatggcat acacaagaat gccacttttt cttttatttc ataccaataa tttaaagatt 2220
gatatgctaa aaacaatttg cacagcacta aagcatgagc tactttcatc taaacctgta 2280

```

```

aaaatatgaa agatttttat attttttcac tgggaagaaa ttcttcctgg atgaaattac 2340
aaatatgtgt agaatatatt taataaaaga cttataaaat acctaactac aggacttaaa 2400
atatagattg gcgcgtagta tatagaacaa tattecatat aaataagttt agcctttata 2460
aaaatgaagt tgcaggctga cattacattc tgtacttact aagtgtcaac agcccttaca 2520
aacattaaat gtaaattggt tcaaatgggtc agcgttggtt aaatgtaatc atgttatatt 2580
attcattggt aatgctttga tgaaaaggct ttatatgcag tagatctacg aaaatattgt 2640
tcatactgat cagaattaaa tttgtataga gcagagtttt aaaatgaatg taaatagcac 2700
taaacgtttt ctttctgcaa cctgtactta cagattcttc ctgtaaacta aataaaaaaa 2760
aaatgatagt gcaaaaaaaa aaaaaaaggg cgccgcctcg cgatctagaa ctagt      2815

```

<210> 218

<211> 1645

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (347)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1643)

<223> n equals a,t,g, or c

<400> 218

```

gcccacgcgt cccgagggcg gggacaactg ggtcttttgc ggctgcagcg ggcttgtagg 60
tgtccggctt tgctggccca gcaagcctga taagcatgaa gctcttatct ttggtggctg 120
tggtcgggtg tttgctggtg ccccagctg aagccaacaa gagttctgaa gatatccggt 180
gcaaattgcat ctgtccacct tatagaaaca tcagtgggca catttacaac cagaatgtat 240
cccagaagga ctgcaactgc ctgcacgtgg tggagcctcat gccagtgcct ggccatgacg 300
tggaggccta ctgcctgctg tgcgagtga ggtacgagga gcgcagnacc accaccatca 360
aggatcatcat tgtcatctac ctgtccgtgg tgggtgccct gttgctctac atggccttcc 420
tgatgctggt ggacctctct atccgaaagc cggatgcata yactgagcaa ctgcacaatg 480
aggaggagaa tgaggatgct cgtcttatgg cagcagctgc tgcaccctc gggggacccc 540
gagcaaacac agtcctggag cgtgtggaag gtgccagca gcggtggaag ctgcagggtgc 600
aggagcagcg gaagacagtc ttcgatcggc acaagatgct cagctagatg ggctgggtgtg 660
gttgggtcaa ggccccaaca ccatggctgc cagcttcag gctggacaaa gcagggggct 720
acttctccct tccctcggtt ccagtcttcc ctttaaaagc ctgtggcatt tttcctcctt 780
ctccctaact ttagaaatgt tgtacttggc tattttgatt agggaaagagg gatgtggtct 840
ctgatctcyg ttgtcttctt ggtcttttgg ggttgaaggg agggggaagg caggccagaa 900
gggaatggag acattcgagg cggcctcagg agtggatgcg atctgtctct cctggctcca 960
ctcttgccgc cttccagctc tgagtcttgg gaatgttgtt acccttgga gataaagctg 1020
ggtcttcagg aactcagtg ctgggaggaa agcatggccc agcattcagc atgtgttctt 1080
ttctgcagtg gttctttatc accacctccc tcccagcccc agcgcctcag ccccagcccc 1140
agctccagcc ctgaggacag ctctgatggg agagctgggc cccctgagcc cactgggtct 1200
tcagggtgca ctggaagctg gtgttcgctg tcccctgtgc acttctcgca ctggggcatg 1260
gagtgcccat gcatactctg ctgccggtcc cctcacctgc acttgagggg tctgggcagt 1320
ccctcctctc cccagtgtcc acagtcactg agccagacgg tcggttgga catgagactc 1380
gaggctgagc gtggatctga acaccacagc ccctgtactt ggggtgcctc ttgtccctga 1440
acttcgttgt accagtgcac ggagagaaaa ttttgcctc ttgtcttaga gttgtgtgta 1500

```

166

```
aatcaaggaa gccatcatta aattgtttta tttctctcaa aaaaaaaaaa aaaaaaccaa 1560
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
aaaaaaaaaa aaaaaaaaaa aangg 1645
```

```
<210> 219
<211> 478
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc feature
<222> (344)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (415)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (452)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (469)
<223> n equals a,t,g, or c
```

```
<400> 219
tcgacccacg cgtccgggga attcaaggag acgggggcga cgcggctgct ggcgcctcct 60
cgggtttggg gctgccgcca tcatgccggg gatagtggag ctgcctactc tggaggatct 120
gaaagtgcag gaggtgaaag tcagttcttc ggtgctcaaa gctgccgccc atcactatgg 180
agttcagtgt gacaagccca acaaggagtt catgctctgc cgctgggaag aaaaagaccc 240
ccggcggtgt ttagaggaag gcaagctcgt caacaaktgt gctctggayt tcttcaggca 300
gataaagctt tcaactgtgca gagcctttta cagactattg gacntgcac gactactccg 360
gcctgcagtg ttttcgtcgc tgccgcaaac agcaggccaa tttgacgatg tgtgnggggc 420
aactgggatg gtgcggctga actggggaaa angttccagt caccaaattg aaaacagt 478
```

```
<210> 220
<211> 832
<212> DNA
<213> Homo sapiens
```

```
<400> 220
atcttagtag agacaagggt tcaccatggt ggccaggctg gtctcgaact cctggcctca 60
ggtgatccac ctgccttggc ctcccaaagt gctccgatta cagggtgkgag ccacccggcc 120
cagcccctcc cttgtgtttc aaccaatcgg aagtgaattt aactagatgt agtaaccttt 180
ttttcttta cttctaaaaa agttacagtt tactaataaa gttaagtctg gttctgtcct 240
agaggaaata aattcactat taattcatgt cttaagttac ttgggttaaa acactttcag 300
ccaccagat taattaaagt ggagcagtggt agcccctggc tgggagatgg cctccagagg 360
```

```

agcagctgca gggcaygttc tgggcttagc gacagaggca agcaagggac tgggtgtctct 420
ggtgagaggt gggtttgatg tatctctgtc ctatgctggc ctctcttctc ctttataaaa 480
tcctctgtgg tcaactgact actgcgtatc gcagtggaaat aagactgcac agttgctggg 540
aggtgagttt aaagtcttaa tctatgcatt cagagaaaata tttttatatg ctttgtgtaa 600
tttataacaa ggattttttt tttagctttg ttaactgtga attcaccctt cctcctccac 660
tgcatattta aagcatgtgt tcacactgtg tgtaaacatt cactgaagat tttttctttg 720
tgcatgtctg actgttcaaa cataacaagt attattaaaa ttaaatatta actgacaaaa 780
aaaaaaaaaa aaaactcgag gggggggccc gtaccaatt cgcccggagt ag 832

```

<210> 221

<211> 1892

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1892)

<223> n equals a,t,g, or c

<400> 221

```

tgactctggg cttagacact cccaacaga gctgaggcca aggccgactc cccctctcaa 60
atggcggtgt ctgggcctat gacggccctt gcagtggagt ctgtactggc tgcgggggac 120
cctgtctcatt tgaatatctg acatcagctg ggcagtcgcc cccctcctcc tttcctccct 180
ctactctgac acagcactta gcacctgaat cttcgtttct ctcccaggga ccttccattt 240
tccatatcca ggaatatgtg atgcgccaca ggtatcagcg tctggwtcgc cacttcacgt 300
tttagccaca agtgactcag tggaagatcc agagtcaaca gaggtcgtc aggaagatgt 360
ctacagaaaa ggtagaccaa aaggaggaa gctgggaaaa agaggtgtgc ggagaccaga 420
tcaaaggacc ggacaagag gaggaaccac cagctgctgc atcccatggc caggggtggc 480
gtccaggtgg cagagcagct aggaacgcaa ggcctgaacc tggggccaga caccctgctc 540
tcccggccat ggtcaacgac cctccagtag ctgccttact gtgggccag gaggtgggac 600
aagtcttggc aggccgtgcc cgcagctgct gctgcagttt ggggtgctct tctgcacat 660
cctccttttg ctctgggtgt ctgtcttctt ctatggctcc ttctactatt cctatatgcc 720
gacagtcagc cacttcagcc ctgtgcattt ctactacagg accgactgtg attcctccac 780
cacttcactc tgctccttcc ctgttgccaa tgtctcgctg actaaggggt gacgtgatcg 840
gggtgtgatg tatggacagc cgtatcgtgt taccttagag cttgagctgc cagagtcctc 900
tgtgaatcaa gatttgggca tgttcttggc caccatttcc tgctacacca gaggtggccg 960
aatcatctcc acttcttctc gttcgggtgt gctgcattac cgctcagacc tgctccagat 1020
gctggacaca ctggtcttct ctacccctct gctatttggc tttgcagagc agaagcagct 1080
gctggaggtg gaactctacg cagactatag agagaactcg tacgtgccga ccactggagc 1140
gatcattgag atccacagca agcgcatcca gctgtatgga gcctacctcc gcatccacgc 1200
gcacttcaat gggctcagat acctgctata caacttcccg atgacctgcg ccttcatagg 1260
tgttgccagc aacttcacct tctcagcgt catcgtgctc ttcagctaca tgcagtgggt 1320
gtgggggggc atctggcccc gacaccgctt ctctttgcag gttaacatcc gaaaaagaga 1380
caattcccg gagggaagtcc aacgaaggat ctctgtcat cagccagggc ctgaaggcca 1440
ggaggagtca actccgcaat cagatgttac agaggatggg gagagccctg argatccctc 1500
agggacagag ggtcagctgt ccgaggagga gaaaccagat cagcagcccc tgagcggaga 1560
agaggagcta gagcctgagg ccagtgtggg ttcaggctcc tgggaagatg cagctttgct 1620
gacggaggcc aacctgcctg ctccctgctc tgcctctgct tctgcccctg tcctagagac 1680
tctgggcagc tctgaacctg ctgggggtgc tctccgacag cgcctccact gctctagttc 1740
ctgaagaaaa ggggcagact cctcacattc cagcactttc ccacctgact cctctccctt 1800
cgtttttctt tcaataaact attttgtgtc agcttcaaaa aaaaaaaaaa aaaaaaaaaa 1860

```

aaaaaaaaa aaaaaaaaaa aaaaaaaaaa an

1892

&lt;210&gt; 222

&lt;211&gt; 868

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (23)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (31)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (45)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (829)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (860)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 222

```
ntttcagcag ttccgcatgc ccntccgtgg naagcctgtt cgtgntattg ggcaagaacc 60
cccatgatgc ccaaggccat ccaagggcat ctgaagacca acccagctct ggaaaacctg 120
ttacttcata tccgggggaa tgtggctttg tgttcaccaa ggaggcctca cttgagatca 180
gggacatgct gctggccaat aaggtgccag ctgccgcccg tgctgggtgcc atagccccc 240
gtgaggtcac tgtgccagcc cagaacactg gtctggggcc cgagaagacc tccttcttcc 300
aggctttagg catcaccact aaaatctcca gaggaacctat tgaaatcctg agtgatgtgc 360
agctgattaa gaccggagac aaagtgggag ccagtgaagc cacactgctg aacatgctga 420
acatctcccc cttctccttt gggetgatca tccagcaggt gtttgacaat ggcagcatct 480
acaaccctga agtgcttgac atcacagagg aaactctgca ttctcgttc ctggaggggtg 540
tccgcaatgt tgccagcgta tgtctgcaga taggttaccc aactgtggca tcagtgtccc 600
attctatcat caatggatac aagcgggtcc tggctttgtc tgtggagact gattacacct 660
ttccacttgc tgaaaaggtc aaggccttct tggctgatcc atctgcattt gtggctgctg 720
ccctgtggc cgtgccacc actgctgcac ctgctgctgc tgcagcccca gccaaagttg 780
```

aagcaaagga agagtcggag gaawcggatg agagkattkt camttcgana atcagcaaaa 840  
gcaacaattc cagccagttt attgtgaa 868

<210> 223

<211> 1516

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1493)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1497)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1508)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1509)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1516)

<223> n equals a,t,g, or c

<400> 223

gaatgagcag gataactgtg tcctgattca tgatgtggac caaaggaaca gcgataaaga 60  
tatctttggg gatgcctgtg ataactgcct gagggtctta rataacgacc agaaagacac 120  
cgatggggat ggaagaggag atgcctgtga tgatgacatg gatggagatg gaataaaaaa 180  
cattctggac aactgccc aaatttccaa tcgtgaccaa cgggacaagg atgggtgatgg 240  
tgtgggggat gcctgtgaca gttgtcctga tgtcagcaac cctaaccagt ctgatgtgga 300  
taatgatctg gttggggact cctgtgacac caatcaggac agtgatggag atgggcacca 360  
ggacagcaca gacaactgcc ccaccgtcat taacagtgcc cagctggaca ccgataagga 420  
tggaattggt gacgagtgtg atgatgatga tgacaatgat ggtatcccag acctggtgcc 480  
ccctggacca gacaactgcc ggctgggtccc caaccagacc caggaggata gcaacagcga 540  
cggagtggga gacatctgtg agtctgactt tgaccaggac cagggtcatcg atcggatcga 600  
cgtctgcccaga gagaacgcag aggtcaccct gaccgacttc agggcttacc agaccgtggt 660  
cctggatcct gaaggggatg cccagatcga tcccactgg gtggctcctga accagggcat 720  
ggagattgta cagaccatga acagtgatcc tggcctggca gtgggggtaca cagcttttaa 780  
tggagttgac ttcgaaggga ccttccatgt gaatacccag acagatgatg actatgcagg 840  
ctttatcttt ggctaccaag atagctccag cttctacgtg gtcatgtgga agcagacgga 900  
gcagacatat tggcaagcca ccccatccg agcagttgca gaacctggca ttcagctcaa 960  
ggctgtgaag tctaagacag gtccagggga gcatctccgg aactccctgt ggcacacggg 1020

```

ggacaccagt gaccagggtca ggctgctgtg gaaggactcc aggaatgtgg gctggaagga 1080
caagggtgtcc taccgctggg tcctacagca caggccccag gtgggctaca tcagggtacg 1140
atattatgaa ggctctgagt tgggtggctga ctctggcgtc accatagaca ccacaatgcg 1200
tggaggccga cttggcggtt tctgcttctc tcaagaaaac atcatctggt ccaacctcaa 1260
gtatcgctgc aatgacacca tccctgagga cttccaagag tttcaaaccg agaatttcga 1320
ccgcttcgat aattaaacca aggaagcaat ctgtaactgc ttttcggaac actaaaacca 1380
tatatatattt aacttcaatt ttcttttagct tttaccaacc caaatatatc aaaacgtttt 1440
atgtgaatgt ggcaataaag gagaagagat cattttttaa aaaaaaaaaa aanttcnggg 1500
gggcccgnnc caattn 1516

```

<210> 224

<211> 1306

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (148)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (887)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1242)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1264)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1303)

<223> n equals a,t,g, or c

<400> 224

```

gtccgcgcgg gcctcggacc tgggggcccc ccggacgtgg acgggggcgg cggcggggcc 60
ccggactccg tcggcgcaca tccccgtccc agcgcagaga gccaccccag gaaaagcccg 120
gctggacgag gtcattggctg ccgctgcnst tacaagcctg tccaccagcc ctctccttct 180
gggggccccg gttgcagcct tcagcccaga gcctggcctg gagccctgga aggaggccct 240
ggtgcggccc ccaggcagct acagcagcag cagcaacagt ggagactggg gatgggacct 300
ggccagtgcg cagtccctctc cgtccacccc gtcaccccca ctgccccccg aggcagccca 360
ctttctgttt ggggagccca ccctgagaaa aaggaagagc ccggcccagg tcatgttcca 420
gtgtctgtgg aagagctgcg ggaaggtgct gagcacggcg tcggcgatgc agagacacat 480
ccgcctggtg cacctgggga ggcaggcaga gcctgatcag agtgatgggt aggaggactt 540
ctactacaca gagctggatg ttggtgtgga cacgctgacc gacgggctgt ccagcctgac 600

```



```

tccagtgtcc cccacggcct ccatgccgcc tgccttcccc cgcctggagc tgccagagct 660
gctggagccc ccagccctgc ctagtcccct gcggccgcct gccccgcccc tgcccccgcc 720
ccctgtcctg agcaccgttg ctaacccccca gtcctgtcac agtgaccgtg tctaccaggg 780
ctgccctgacg cccgcccgcc tggagccgca gcccacggag gtcggagcct gccacccgc 840
cttgtcctcc aggatcggag tcacctgag gaagccccgc ggcgacnsaa agaagtgccg 900
gaaggtgtat ggcatggagc gccgggacct ctggtgcaca gcctgccgct ggaagaaagc 960
ctgccagcgg ttcctggact aagtccggct cgttcaagaa cataagctac caccttctcc 1020
ctccccaccc cctccaggcc cggggctgaa acagcccag grcagcccca ggggctggcc 1080
ttcaccagct gcagggctctg cttttacttg ggggtggggg gcggggctga cctgaaccc 1140
tccccccgc caggtcgggg aggggtccca mactcaaag tgcttctaaa gaaaccagct 1200
ttttgcact aaaagccaaa acaaaacggt gttcccttta gncccaagg ggccttgggg 1260
gcanccaacc ttcccgggct tgttggggcc cgtaagattt ttnttc 1306

```

&lt;210&gt; 225

&lt;211&gt; 584

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (486)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (542)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (562)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 225

```

tcgaccacg cgtccggcgt cctctcggag cccgtgcggt cacttagcca agatgcctga 60
ggaacccag acccaagacc aaccgatgga ggaggaggag gttgagacgt tcgcctttca 120
ggcagaaaty gcscagttga tgcrytgat catcaayacy ttctactcga acaargagat 180
cttcttgccg gactgatctc caactcgtcc gacgctcygg acaaaatccg atacgagagc 240
ctgaccgacc ccagcaagct cgactcgggg aaggagctgc acattaacct catcccgaac 300
aagcaggacc ggacctcac catcgtggga taccgggatc gcatgaccaa ggccgacctg 360
atcaacaacc tgggcaccat cgccaaktcg gggaccaaag cgttcatgga agytctgcag 420
gcgggcgag atatttcyat gattggccag ttcggggctc ggttctattc ggctactttg 480
gtggcnagaa ggtgacggtg atcaccaagc acaacgatga cgagcattac gcctgggagt 540
cntccgcagg ggctcgttca angttccgca ttgacacagt gaac 584

```

&lt;210&gt; 226

&lt;211&gt; 523

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

<221> misc feature  
 <222> (34)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (498)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (514)  
 <223> n equals a,t,g, or c

<400> 226  
 tcgacccacg cgtccgccag cagaaggctg ttgnngggacg tctgccagga ctgcatccag 60  
 atggtgacag acatccagac tgctgtaagg accaactcca cctttgttga agctttggtg 120  
 gaccatgcc aagcacagtg tgatctcctg gggcccggca tggctgacat gtgcaagaac 180  
 tatatcaacc agtattcgga cattgccgtc cagatgatga tgcacatgca acccaaagag 240  
 atctgtggcc tggttgggtt ctgcgaccaa gtgaaggaga tgcccatgca gactctgac 300  
 cctgccaaag cgggtctcaga gaacgtcctc cctgcattgg aactggtgga gccattaaag 360  
 aaggacacgg tccaggcaaa gaccagtgtt agctgtggag atatgagagt tacgtggttg 420  
 aaggaaagtg ccaagctcca ttggacaaca acaggactga ggaagaaata gtttcaggct 480  
 tggataaatg tgctccantt gccctaagtc ctanctgaac atg 523

<210> 227  
 <211> 2377  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (2369)  
 <223> n equals a,t,g,, or c

<400> 227  
 gccgatcccg gagtcggagc cgttccaggt ctgcagccg atctcgctac agccgctcga 60  
 agtctcggtc ccgcactcgt tctcgatctc ggtcgacctc caagtccaga tccgcacgaa 120  
 ggtccaagtc caagtcctcg tcggtctcca gatctcgttc gcggtccagg tcccggctctc 180  
 ggtccaggag tcctcccca gtgtccaaga gggaatccaa atccaggctc cgatcgaaga 240  
 gtccccccaa gtctcctgaa gaggaaggag cgggtgcctc ttaagaaaat ggtaatgtct 300  
 gggaatccga gacacataac cctaattcat aaatgggatt tggggtaggc ctttttgagt 360  
 cgtgttaatg taagaatgac tcctatcatt aggagtgtc ctccggagggt actcaccttt 420  
 gggagtaata ctgaagagag ggggtctgcag aaaggatgtg tatgaagctt agataataat 480  
 ggctgtttcg taaactgttt gagacctatt aatgaaaatg actatttctt gctgttttta 540  
 tccaacgtct gcattttccc cctttaaagc tgcggtctcc tgtttgataa agaataattg 600  
 gccagtattg cagattttta ctgatttggc tgatcctcca gggaccagtt tctgtgggag 660  
 tgtattggar caggtttgtc tttaaatgtt aaagatgcac tatcctctta gagaaacaat 720  
 cagttcaact attgttgtac tgactgggac ttcatttctt aatggatgtg gcaaaagaat 780  
 tgcaataaga agcagtgaac atttgaacc ccaaaagaaa gttacaggta ttgactggg 840  
 tggggaaagg atagtgtgtc ttttaactctt aaattgtttg gtcctatttt ttaaaaaagg 900

```

aagggcccta agtagctcag atattaaagt agtattctca attaccaaatt gtttcatttg 960
aaacaatttta tcttaatgaa atatatagacca attctctgat ctcgagttgt ttttgtttgg 1020
atacagccct ttttttttcc ttttttttcc ttcccttac ctttcttcac cttgggtatt 1080
tgggccaggaa tacgtaaatt caaacttgta catgctgatg gtagcctttg tgaaattttc 1140
ctaattgggc cttttaaaaa catggctggg tggaaacatt ctgtacccta ctgggttgac 1200
cagagcctta gtaagtacgt gcctgaaact gaaaccatgt gcactttaat ggaaggttaag 1260
ctgaacttct tctttttcaa acctagatgt atcggcaagc agtgtaaagc gaggacttgg 1320
ggaaaaagga ccacatagtc catcgaagaa gagtccttgg aacaagcaac tggctattga 1380
aaaggttatt ttgtaacatt tgtctaactt tttacttggt taagctttgc ctcagttggc 1440
aaacttcatt ttaigtgcca ttttggtgct gttattcaaa tttcttgtaa tttagtggg 1500
tgaacgactt cagatttcat tattggattt ggatatttga ggtaaaattt cattttgtta 1560
tatagtgctg actttttttg tttgaaatta aacagattgg taacctaat tgtggcctcc 1620
tgacttttaa ggaaaacgtg tgcagccatt acacacagcc taaagctgtc aagagattga 1680
ctcggcattg ccttcattcc ttaaaattaa aaacctacaa aagttggtgt aaatttgat 1740
atgtatttta ccttcagatc taaatggtaa tctgaaccca aatttgata aagacttttc 1800
aggtgaaaag acttgatttt ttgaaaggat tgtttatcaa acacaattct aatctcttct 1860
cttatgtatt tttgtgcact aggcgcagtt gtgtagcagt tgagtaatgc tggtagctg 1920
ttaaggtggc gtgttgcatg gcagagtgtc tggctgtttc ctgttttctc ccgattgctc 1980
ctgtgtaaag atgccttgct gtgcagaac aaatggctgt ccagtttatt aaaatgcctg 2040
acaactgcac ttccagtcac ccgggccttg catataaata acggagcata cagtgaacac 2100
atctagctga tgataaatat accttttttt cctcttctcc cctaaaaatg gtaaatctga 2160
tcatatctac atgtatgaac ttaacatgga aaatgttaag gaagcaaatg gttgtaactt 2220
tgtaagtact tataacatgg tgtatctttt tgcttatgaa tattctgtat tataaccatt 2280
gtttctgtag ttttaattaaa acattttctt ggtgttagct tttctcagaa aaaaaaaaaa 2340
aaaaaaaaaa aaaaaaaaaa aaaaaaaang aaaaaag 2377

```

&lt;210&gt; 228

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 228

```

aatacatgcc aaatggatca ttaaatgaac tcctacatag gaaaactgaa tctcctgatg 60
ttgcttggcc attgagattt cgcacccctg atgaaattgc ccttggtgta aattacctgc 120
acaatatgac tctccttta cttcatcatg acttgaagac tcagaatatc ttattggaca 180
atgaatttca tgtaagattt gcagattttg gtttatcaaa gtggcgcatg atgtccctct 240
cacagtcacg aagtagcaaa tctgcaccag aaggaggagc aattatctat atgccacctg 300
aaaactatga acctggacaa aaatcaaggg ccagtatcaa gcacgatata tatagctatg 360
cagttatcac atgggaagtg ktatccagaa aacagccttt tgaagatgtc accaatcctt 420
tcagataat gtatagtgtg tcacaaggac attggactgg tat 463

```

&lt;210&gt; 229

&lt;211&gt; 1232

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 229

```

caggtgagca tctgaacaag gggcagtcgg ccagggtggg cttgcgggag tccccacctt 60
gacctctctc ccttccagct gccacagacc cagaccaagc atggacgccg tggatgccac 120
catggagaaa ctccgggcac agtgccctgt ccggggggcc tcgggcatcc agggcctggc 180
caggtttttc cgccaactag accgggacgg gagcagatcc ctggacgctg atgagttccg 240

```

```

gcaggggtctg gccaaactcg ggctgggtgct ggaccaggcg gaggcagagg gtgtgtgcag 300
gaagtgggac cgcaatggca gcgggacgct ggatctggag gagttccttc gggcgctgcg 360
gccccccatg tcccaggccc gggaggctgt catcgagct gcatttgcca agctggaccg 420
cagtggggac ggcgtcgtga cggtaggacga cctccgcggg gtgtacagtg gccgtgacca 480
ccccaaagtg cgcagtgggg agtggaccga ggacgaggtg ctgcgcgct tcctggacaa 540
cttcgactcc tctgagaagg acgggcaggt cacactggcg gaattccagg actactacag 600
cggcgtgagt gcctccatga acacggatga ggagttcgtg gccatgatga ccagtgcctg 660
gcagctgtga gcagctccgg ctacagccctg ctgccctggc ctgtcactyc ccacccctgc 720
cggagacctc ccttccttg gccccttctc ttctgggcag scacaccaca gagcggggag 780
gggcaggtgg gggaatggag gctgcaggac tggttagacc aggtccctgc cggccacca 840
ggcggagggtg ggacaaaggt cctaacagga gtcactggct caggacccca gggagaaacg 900
ctctcccccac ccacgcatg ctgaccagag gtcttgacgc ccctgtggat gcccgcgcg 960
aggtcccccg atcccccgc cggactgct gctccctgccc cctcccttgc gggccccca 1020
ggaagccagg tgacccagg tgggaggctg tgtgtggagg ccattcctgga aggaagtta 1080
gacctgcccga ggtgtggagc gaggggcaca ggggcatcct aacctcagaa actgaaataa 1140
agcctttgaa aaaaaaatct gtaaaacatc aacccccaat cagaagatgg caaatgggga 1200
ataaaaatag caggtaacac gtcaaaaaaa aa 1232

```

&lt;210&gt; 230

&lt;211&gt; 1063

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 230

```

gcccacgcgt ccgctcagcg gctgccaaaca gatcatgagc catcagctcc tctggggcca 60
gctataggac aacagaactc tcaccaaagg accagacaca gtgggcacca tgggacagt 120
tcggctagcc aacgcagagg atgctcagga attcagtgat gtggagaggg ccattgagac 180
cctcatcaag aactttcacc agtactccgt ggagggtggg aaggagacgc tgaccccttc 240
tgagctacgg gacctggtca cccagcagct gcccctctc atgccgagca actgtggcct 300
ggaagagaaa attgccaaacc tgggcagctg caatgactct aaactggagt tcaggagt 360
ctgggagctg attggagaag cggccaagag tgtgaagctg gagaggcctg tccgggggca 420
ctgagaactc cctctggaat tcttgggggg tgttggggag agactgtggg cctggaaata 480
aaacttgtct cctctaccac caccctgtac cctagcctgc acctgtccwc atctctgcaa 540
agttcagctt ccttccccag gtctctgtgc actctgtctt ggatgctctg gggagctcat 600
gggtggagga gtctccacca gagggaggct caggggactg gttgggccag ggatgaatat 660
ttgagggata aaaattgtgt aagagccaaa gaattggtag tagggggaga acagagagga 720
gctgggctat gggaaatgat ttgaataatg gagctgggaa tatggctgga tatctgttac 780
taaaaaaggg tctttaagaa cctacttcct aatctctcc ccaatccaaa ccatagctgt 840
ctgtccagtg ctctcttcct gcctccagct ctgcccaggg ctctctctar actctgtccc 900
tggtgctagg caggggagga gggagagcag ggttggggga gaggtgagg agagtgtgac 960
atgtggggag aggaccagct ggggtgcttg gcattgacag aatgatggtt gktttgatc 1020
atgtgattaa taaaaaaaaa tgaaaaaagt gaaaaaaaaa aaa 1063

```

&lt;210&gt; 231

&lt;211&gt; 1063

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1056)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1061)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1063)

<223> n equals a,t,g, or c

<400> 231

```

gatcaccacc agggagcaga atccgttcca gggattgggg tgagtccgac ttcgagcagc 60
agctgcccc caacatcatg taccagccc gtgactacgt ggagccctgg gcttcgcgta 120
gagtccttag acggggcgaa aacgggaaaa ggggccttaa ctggggcacc tggctccttt 180
gggagctcgg agtttctgac tggcctgcgc aacacctcag aggcaaggkg aacgcgaggg 240
cctataatgc aagaaccaag gcgagtcacg ccctgtctgg gcaaaagagg agtaaagacc 300
cctcagctgc agcccggcag cgcattccta ccaggggtcc gccgccagag ctttcccgcg 360
cggtcggata gttacactac tgtccgggac ttcctagccg tgccgcggac catctcaagt 420
gcttcgcgca cactcatcat ggcggtggca gtaagtcact tccgcccggg accggaartg 480
tgggatactg cgagtatggc ggcgtcaaag gtgaagcagg acatgcctcc gccggggggc 540
tatgggcccc tcgactacaa acggaacttg ccgcgtcgag gactgtcggg ctacagcatg 600
ctggccatag ggattggaac cctgatctac gggcactgga gcataatgaa gtggaaccgt 660
gagcgcaggc gcctacaaat cgaggacttc gaggctcgca tcgcgctgtt gccactgtta 720
caggcagaaa ccgaccggag gaccttgacg atgcttcggg agaacctgga ggaggaggcc 780
atcatcatga aggacgtgcc cgactggaag gtgggggagt ctgtgttcca cacaaccgcg 840
tgggtgcccc ccttgatcgg ggagctgtac gggctgcgca ccacagagga ggctctccat 900
gccagccacg gcttcatgtg gtacacgtag gccctgtgcc ctccggccac ctggatccct 960
gcccctcccc actgggacgg aataaatgct ctgcagacct gaaaaaaaaa aaaaaaaaaa 1020
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaanaaaa nan 1063

```

<210> 232

<211> 1474

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1337)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1359)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1377)

<223> n equals a,t,g, or c

&lt;400&gt; 232

```
ggattcctac cctcatcacg gcctttgtcc ttgtacctc tcaggcccaa gctggatggc 60
tgcaacatga ttatggccac ctgtctgtct acagaaaacc caagtggaac caccttgtcc 120
acaaattcgt cattggccac ttaaagggtg cctctgccaa ctggtggaat catcgccact 180
tccagcacca cgccaagcct aacatcttcc acaaggatcc cgatgtgaac atgctgcacg 240
tgtttgttct gggcgaatgg cagcccatcg agtacggcaa gaagaagctg aaatacctgc 300
cctacaatca ccagcacgaa tacttcttcc tgattgggcc gccgctgctc atccccatgt 360
atttcagta ccagatcatc atgaccatga tcgtccataa gaactgggtg gacctggcct 420
gggccgtcag ctactacatc cggttcttca tcacctacat ccctttctac ggcatcctgg 480
gagccctcct ttctctcaac ttcatcaggt tcctggagag ccactggttt gtgtgggtca 540
cacagatgaa tcacatcgtc atggagattg accaggaggc ctaccgtgac tggttcagta 600
gccagctgac agccacctgc aacgtggagc agtccttctt caacgactgg ttcagtggac 660
accttaactt ccagattgag caccacctct tccccaccat gccccggcac aacttacaca 720
agatcgcccc gctggtgaag tctctatgtg ccaagcatgg cattgaatac caggagaagc 780
cgctactgag ggccctgctg gacatcatca ggtccctgaa gaagtctggg aagctgtggc 840
tggaagccta ccttcacaaa tgaagccaca gcccccggga cacygtgggg aagggtgca 900
ggtgggggtg tggccagagg aatgatgggc ttttgttctg aggggtgtcc gagaggctgg 960
tgtatgact gtcacggac cccatgttg atctttctcc ctttctcctc tcctttttct 1020
cttcacatct ccccatagc acctgcct catgggacct gccctccctc agccgtcagc 1080
catcagccat ggccctccca gtgcctccta gccccttctt ccaaggagca gagagggtggc 1140
caccgggggt ggctctgtcc tacctccact ctctgccct aaagatggga ggagaccagc 1200
ggtccatggg tctggcctgt gagtctcccc ttgcagcctg gtcactaggc atcacccccg 1260
ctttggttct tcagatgctc ttggggttca targggcarg tcctagtctg ggccarggcc 1320
ctgacctcc cggttngct taaatctccc tgaacggtng caattggtcc acctttncat 1380
aaaaaaggct gcttgttaca aagtctgggt tttccttct gcaactcggg taataaccga 1440
aggctctctt aagatgttca agggcccaag gccg 1474
```

&lt;210&gt; 233

&lt;211&gt; 1782

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (8)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (31)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (34)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (591)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1760)

<223> n equals a,t,g, or c

<400> 233

```
aagatganag gctcacccta aaacatcttc ntnctctac cagtgagact atcaaccatg 60
gatctatcta tctatttttt aagcctgcat cacttcttga gataatgagg tttctacctc 120
caaagcctgc tgggtgagca ccttgctcat tatactggwt ctgaatttac ctctttgaag 180
tttctagatg caccacttcc tgctcacagc ctggaattcg gttaacaagt cagtgtcaac 240
ctacctttcc cttcatgatt tatagacttt tgggagtacc ttctggtagc ttttgtcttc 300
ccataggaaa gaggcccaat cccagtttgt cctcacaagg cggccagctc cgtgatatct 360
cttttgccgg cagagttaaag attgtacaca gatccccaca agtaccacgr tttttgcctc 420
aggaaggata aagcacatgt ttgtttctgc ttctgttttc tttttcttt ttttcasgaa 480
gccttatgga gaagtatgtt tctgctttct ttctgrgga agcctagytt ctgggccacg 540
ggactgatcc tgtctacatc ctctttccct ccattctcca tcgtgtctct ncccccgctc 600
caccaccacc gtgccctctc ytgscctcagc ttccctctt cccctgcagt gaggttcctg 660
cgcagcggca ctaagctcat cttccgcctg aggcctaggc agaaggaaagc tggcctgagc 720
caatcacacg atgacctctc caacgcaacg gccacgcca gtgtccgaaa gaaggccggc 780
agcttttctc gccgccttat caagcgcttt tcttcaaat ccaaacccaa ggccaatggt 840
aaccaccagc cccagctctg aggaccacgc tctgaaaggg cagagattct ctcagcccat 900
tccccacctc ccttccata ccccttctg gatctccagt gcctgggcca ggaaagccct 960
ctgggttccg ggaagccccg tccacctgg gccatggggc cgggtggaag gatacttga 1020
acgggaagca catgagaggg gggcaccctg tgccgaggac atggacgagg gactggtggc 1080
tgggagggag aggagggccc tgtccggcat gtgtgggtat tccccagaag catttgctc 1140
ctgctgagcc tggctccctga gcggagtccc aggggtgctc gctcttcac tgaccttct 1200
tcccttattt attctctttt ctatttatat gtgtggctta ggaccctccg tgaacagatg 1260
atagagggca tctctcccag gtgaccttc tttctgtcc caggaggggtg ggtaattccc 1320
tttgggatgg ggctcccaca cctccctcag gtcccccactc agaccagcac cagtgtctgc 1380
ctctgagaat gttggcagct cacagagagc agggccggcc cgggatgggg ggaggtact 1440
ccccacctc ctgctcccc tctgtctct catccctccc tcccccttta ttaccgtttt 1500
ttgtacttga tgccttctct gtgagcagtg gctctgtggg aaggagggag ccgggagcct 1560
ggtgggaagc cttccccaga gagatggctt taggggcttt atttaaagac tgtgatgatg 1620
gagccacgca aggctgcacc tctgtgtgtt gggagacgat gatgatgtcc attgctgtgt 1680
gatggcttgg aatttaattt attaaagtca aattggagtt taacacacac aacacacac 1740
aaattcgggg ggggcccctn acccattggc cctaaggggg gg 1782
```

<210> 234

<211> 2208

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1314)

<223> n equals a,t,g, or c

<220>

<221> misc feature

&lt;222&gt; (2189)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (2202)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 234

```
acagggctcg gagccaagct cagagaacgc caatgacacc atcattttgc gcaacctgaa 60
cccacacagc accatggatt ccattcctggg ggccctggca ccctacgcgg tgctgtcctc 120
ctccaacgtg cgcgtcataa aggacaagca gacccaactg aaccgcggct ttgccttcat 180
ccagctctcc accatcgagg cagcccagct gctgcagatc ctgcaggccc tgcaccaccc 240
actcactatc gacggcaaga ccatcaatgt tgagtttgcc aagggttcta agagggacat 300
ggcctccaat gaaggcagtc gcatcagtcg tgcctctgtg gccagcactg ccattgctgc 360
ggcccagtg gcatctcac aggcctccca aggtggggag ggtacctggg ccacctccga 420
ggagccgccc gtcgactaca gctactacca acaggatgag ggctatggca acagccaggg 480
cacagagtct tccctctatg cccatggcta cctcaagggc accaagggcc ctggcatcac 540
tggaaccaa ggggatccca ctggagcagg tcccagggcc tccctagagc ctggggccga 600
ctctgtgtcg atgcaggctt tctctcgcgc ccagcctggt gctgctcctg gcatctacca 660
acaatcagcc gaggcgagca gtagccaggg cactgctgcc aacagccagt cgtataccat 720
catgtcaccg gctgtgtcga aatctgagct ccagagccct acccattcta gttctgctct 780
cccaccggct accagcccca ctgcccagga atcctacagc cagtaccctg ttcccagcgt 840
ctctacctac cagtacgatg agacctccgg ctactactat gacccccaga ccggcctcta 900
ctatgacccc aactcccagt attactacaa tgctcagagc cagcagtacc tgtactggga 960
tggggagagg cggacctatg ttcccgcctt ggagcagtcg gccgacggac ataaggagac 1020
aggggcaccc tcgaaggagg gcaaagagaa gaaggagaa cacaagacca agacagctca 1080
acagattgcc aaggacatgg aacgtggggc ccgagtcctc aacaaacaaa aagaaaactt 1140
caaaaatagc ttccagccta tcagctccct gcgagatgac gagaggcggg agtcagccac 1200
tgcatatgct ggctatgcca tcctcgagaa gaaggagca ctagccgaga gacagcacac 1260
cagcatggat ctcccgaat tggccagtga cgaccgccc agccctccgc gagnactggt 1320
ggcagcctac agcggggaga gtgacagtga ggaggagcag gagcgtgggg gccctgagcg 1380
ggaggagaag ctcaccgact ggcagaagct ggctgtctg ctctgccgac gccagtccc 1440
cagcaaagag gcgctcatcc ggcaccagca gctctcagg ctccacaagc aaaaccttga 1500
gattcaccgg cgagcccact tgtcagaaaa cgagctagaa gcaactagaga agaattgacat 1560
ggagcaaatg aagtaccggg accgtgcagc tgaacgcaga gaaaagtatg gcatccccga 1620
gccgccagag cccaagagga ggaagtacgg cggcatatcc acagcctctg tagacttcca 1680
gcagcctact cgggacgggc tgggcagtga caacattggc agtcggatgc tgcaggccat 1740
gggctggaag gagggcagcg gcctgggccg maagaagcag ggcattgtaa cgcctatcga 1800
ggcccaaaca cgggtgcggg gctccggcct gggtgacagg ggcagctcct acggggtcac 1860
ctcaaccgag tctacaagg agacactgca caagacaatg gtgaccgct tcaacgaggc 1920
ccagttagca gcttcaagg caacttctcc acatgttggg tgtccatcct ggggcaggga 1980
aggacagagt gttggatggc tgggacgggg ccttgcctt gtcggccagc cactcccca 2040
gccagagagg gcttgaccaa atcaaattga ggtggtgact tttgttgaa aattgggctg 2100
ggatcacgtc ctgttttgta ataaaagctg aaaagtctga aaaaaaaaa aaaaaaac 2160
ccgggggggg ggcccgtac ccattttcnc cctaaagtga gnggtttt 2208
```

&lt;210&gt; 235

&lt;211&gt; 2580

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens



<220>  
<221> misc feature  
<222> (1)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (3)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2558)  
<223> n equals a,t,g, or c

<400> 235  
ntncacgcgt ccggggcgcc agacccgget ttgccgtccg gctattagcc tactgtggct 60  
agtcaccccc ggggtcccg ccttctcggg ctggggccgc cgccaccgcg gcaggacggg 120  
gaggcgggcc atggcgctct gcgtggggag ccggacccta agcaaggatg atgtgaacta 180  
caaaatgcat ttccgatga tcaacgagca gcaagtggag gacatcacca ttgacttctt 240  
ctaccggccg cataccatca cctgctcag cttcaccatc gtcagcctca tgtacttcgc 300  
ctttaccagg gatgactctg ttccagaaga caacatctgg agaggcatcc tctctgttat 360  
tttcttcttt cttatcatca gtgtgttagc tttccccaat ggtccgttca ctcgacctca 420  
tccagcctta tggcgaatgg tttttggact cagtgtgctc tacttcctgt tcctggattt 480  
cctactcttc ctgaatttcg agcagggtta atctctaag tattggctag atccaaatct 540  
tcgatacgcc acaagggaag cagatgtcat ggagtatgct gtgaactgcc atgtgatcac 600  
ctgggagagg attatcagcc actttgatat ttttgcatth ggacatttct ggggctgggc 660  
catgaaggcc ttgtgatcc gtagttacgg tctctgctgg acaatcagta ttacctggga 720  
gctgactgag ctcttcttca wgcattctct ccccaatttt gccgagtgcg ggtgggatca 780  
agtcattctg gacatcctgt tgtgcaatgg cgtgggcatt tggctgggca tggctgtttg 840  
ccgtttttta gagatgagga cttaccactg ggcaagcttc aaggacattc ataccaccac 900  
cgggaagatc aagagagctg ttctgcagtt cactcctgct agctggacct atgttcgatg 960  
gtttgacccc aaatcttctt ttccagagag agctggagtg taccttttca tgatcatctg 1020  
gcagctgact gagttgaata ccttcttctt gaagcatatc tttgtgttcc aagccagtca 1080  
tccattaagt tggggtagaa ttctctttat tgggtggcatc acagctccca cagtgaagca 1140  
gtactacgct tacctcaccg acacacagtg caagcgcgta ggaacacaat gctgggtgtt 1200  
tggggctcatt ggtttcctgg aggccattgt ttgcataaaa tttggacaag atctcttctc 1260  
taagacccaa atactctatg ttgtgctttg gcttctttgc gtggctttca ccactttcct 1320  
ctgtctgtac ggcattgatt ggtatgcaga acactatggt caccgagaaa agacctactc 1380  
ggagtgtgaa gatggcacct acagtccaga gatctcctgg catcacagga aagggacaaa 1440  
aggttctgaa gacagcccac ccaagcatgc aggcaacaac gaaagccatt cttccaggag 1500  
aagggaatcg cattccaagt caaaagtcac caatggcggt ggaaagaaat gaaaaaccct 1560  
ggttaatcaa agatgttcca gagtgcctag aactgagagg gaaatggaac tcatttgga 1620  
ctccccgtga ggaggtcgag gcgcacaggg caagcaggaa gaggcgaggg cacttggggg 1680  
tcattatttg agatcgtaag tcttgtttcc cacagacctg gccgcgtcag gcagatcatc 1740  
gcctgggggg cctttgccaa cgtggggtct cttctaactt cagcacttga catgcgggtca 1800  
ccgtgggcag cgcggtgtgt tgaagggaaa cgttagctat tcattcacag ttgccaagag 1860  
cagctccgcg cctgctggat cgtggatgca gcgtaaacat cttccttcag acgaggcatt 1920  
aaccctcatg ttaatggact ggtcaccagt ttttatttta tttttatgaa tctacctttc 1980  
cattgattga ttaagtcca ggccactttt ctgtctttta tttggttact gttgttattt 2040

```

gtttttaagt taggatgctt tttaacagcc tttagaagcc gctgctgaaa ttgatactgg 2100
gggaagggtt ccccttcctt ctagagcaga aaaggagag aggtgttgta ttcctgtttg 2160
gtaacctcag tctcctgtaa gacctcctac cacatggcga gtatacacca atcaggagag 2220
ggtagctgcc tgcataggag cctcgcttcc gattattccc tcccaatat tattcatcca 2280
gacttagcca cagtgcacaa aagcaaacct gctagagagg cagtgaacac cacagcttct 2340
ccccagctag gtgcctttta catcggtttt gttctccttc catggtgtgt tgctgacatt 2400
gtcactgagt cccatgtgag gtgctggtga gtattacctt tcatctgtgc catgctctag 2460
aaccttgacc ttgatagtgc accacctctg atggatccct gttttaaata aaaacgattc 2520
actttaaacg ctaaaaaaaaa aaaaaaattg ggggggggnc cgtaacccaa ttggcccttt 2580

```

<210> 236

<211> 3008

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3001)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3008)

<223> n equals a,t,g, or c

<400> 236

```

gtcatcactc tgttgcccag gctggaatgg tgaagtgcag tggcatgata tcggetcagt 60
gcagcctctg tctcccgggt tcaagcgatt ctctgcctc agcctctaaa gagtgtgagg 120
aagaggctgt ctgtgtcatt atgtgtgcgt cgggtcaagta taatatccgg ggtcctgccc 180
tcatcccaag aatgaagacc aagcaccgaa tctactatat caccctcttc tccattgtcc 240
tcctgggcat cattgccact ggcatgtttc agttttggcc ccattctatc gagtctcaa 300
atgactggaa tgtagagaag cgcacatccg tgatgtgccg gttgttaggc tgccagccga 360
cagtcccatc ccagagcggg gggatctcag ttgcagaatg cacacgtgtt ttgatgtcta 420
tcgctgtggc ttcaacccaa agaacaaaat caaggtgtat atctatgctc tgaaaaagta 480
cgtggatgac tttggcgtct ctgtcagcaa caccatctcc cgggagtata atgaactgct 540
catggccatc tcagacagtg actactacac tgatgacatc aaccgggcct gtctgtttgt 600
tccctccatc gatgtgctta accagaacac actgcgcac aaggagacag cacaagcgat 660
ggcccagctc tctaggtggg atcgaggtac gaatcacctg ttgttcaaca tgttgccctg 720
aggtcccca gattataaca cagccctgga tgtcccaga gacagggccc tgttggtg 780
tggtcgcttt tctacgtgga cttaccgga aggctacgat gtcagcattc ctgtctatag 840
tccactgtca gctgaggtgg atcttccaga gaaaggacca ggtccacggc aatacttct 900
cctgtcatct cagggtgggtc tccatcctga gtacagagag gacctagaag ccctccaggt 960
caaacatgga gagtcatgtg tagtactcga taaatgcacc aacctctcag aggggtgtcct 1020
ttctgtccgt aagcgtgcc acaagcacca ggtcttcgat taccacagag tgctacagga 1080
ggctactttc tgtgtggttc ttctgtggag tcggtggggc caggcagtat tgagcgatgt 1140
gttacaagct ggctgtgtcc cggtgtcatc tgcagactcc tatattttgc ctttctctga 1200
agttcttgag tgaagagag catctgtggt tgtaccagaa gaaaagatgt cagatgtgta 1260
cagtattttg cagagcatcc cccaaagaca gattgaagaa atgcagagac aggcccggtg 1320
gttctgggaa gcgtacttcc agtcaattaa agccattgcc ctggccaccc tgcagattat 1380
caatgaccgg atctatccat atgctgcatc ctctatgaa gaatggaatg accctctgc 1440
tgtgaagtgg ggcagcgtga gcaatccact cttctcccg ctgatccac cacagtctca 1500

```

```

agggttcacc gccatagtcc tcacctacga ccgagtagag agcctcttcc gggcatcac 1560
tgaagtgtcc aagggtgccca gtctatccaa actacttgct gtctggaata atcagaataa 1620
aaacctctca gaagattctc tctggcccaa aatccgggtt ccattaaaag ttgtgaggac 1680
tgctgaaaac aagttaagta accgtttctt cccttatgat gaaatcgaga cagaagctgt 1740
tctggccatt gatgatgata tcattatgct gacctctgac gagctgcaat ttggttatga 1800
ggtctggcgg gaatttctctg accggttggg gggttaccgg ggtcgtctgc atctctggga 1860
ccatgagatg aataagtga agtatgagtc tgagtggacg aatgaagtgt ccatggtgct 1920
cactggggca gctttttatc acaagtattt taattacctg tataacctaca aaatgcctgg 1980
ggatatcaag aactgggtag atgctcatat gaactgtgaa gatattgccca tgaacttctc 2040
ggtggccaac gtcacgggaa aagcagttat caaggtaacc ccacgaaaga aattcaagt 2100
tcctgagtg acagccatag atgggctttc actagaccaa acacacatgg tggagaggtc 2160
agagtgcac aacaagtttg cttcagtcct cgggaccatg cctctcaagg tgggtgaaca 2220
ccgagctgac cctgtcctgt acaaagatga ctttcctgag aagctgaaga gcttcccaa 2280
cattggcagc ttatgaaacg tgtcattggt ggaggtctga atgtgaggct gggacagagg 2340
gagagaacaa ggcctcccag cactctgatg tcagagtagt aggttaaggg tggaaaggtg 2400
acctacttg atcttggcat gcacccacct aacccacttt ctcaagaaca agaacctaga 2460
atgaatatcc aagcacctcg agctatgcaa cctctgttct tgtatttctt atgatctctg 2520
atgggttctt ctgaaaaatg ccaagtggaa gactttgttg catgctccag atttaaatac 2580
agctgaggct ccttttgttt tcagttccat gtaacaatct ggaaggaaac ttcacggaca 2640
ggaagactgc tggagaagag aagcgtgtta gccatttga ggtctgggga atcatgtaaa 2700
gggtaccag acctcacttt tagttattta catcaatgag ttctttcagg gaaccaaac 2760
cagaattcgg tgcaaaaagc aaacatcttg gtgggatttg ataaatgcct tgggacctgg 2820
agtgtctggc ttgtgcacag gaagagcacc agccgctgag tcaggatcct gtcagttcca 2880
tgagctattc ctctttggtt tggctttttg atatgattaa aattattttt tattcctttw 2940
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3000
nggggggn                                     3008

```

<210> 237

<211> 877

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (834)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (854)

<223> n equals a,t,g, or c

<400> 237

```

caattattga agtcaagtga tgggcacaga ggattgatag ctcaaataag gcttgggtact 60
tgcccttgga aaaagtatgc taggattctg gtgggagggg tagacatata aatggataat 120
ttataatatg atgtaagtac agagagctgt gggaacataa aggaaggaaa atgaacttga 180
gtctgagact gctcacttct attagagccc tcttctgttt tgcttcatgt tcagccttca 240
ggaagaactc atttctgttg ttgacaactg aagttgtctg tcagaaagca atgttgtaag 300
gtgacgtaca gctacatatt tttcctcaaa attgaggtga aaggaaattc taaagtaggc 360
attatgttct taatttttat ctgtgaatta agccaccag ctctcagct ctttctctgt 420
tggccctcta cttcagatta ctttctatga agacaaaaat tttcaaggcc gtcgctatga 480

```

```
ctgtgattgc gactgtgcag atytccacac atacctaaagt cgctgcaact ccattaaagt 540
ggaaggaggc acctgggctg tttatgaaag gcccaacttt gctgggtaca tgtacatctt 600
accacaggga gagtaccctg aataccagcg ttggatgggc ctcaacgacc gcctcagctc 660
ckgcagagct gtttcacctg cctagtggag gccagtataa gattcagatc tttgagaaag 720
gggatttttag tggtcagatg tatgaaacca ccgaagattg cccttccatc atggagcatt 780
tcacatgcga gagaccatcc tgtaagtgtc ggaggtgtct ggattttcta tgancatccc 840
aactaccgtg gcangcagta ctcctggaca agaagga 877
```

<210> 238

<211> 3039

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (170)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (177)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3039)

<223> n equals a,t,g, or c

<400> 238

```
ccgatgccga cctggctcgc tgggaccccg acagcgtaa aaccatctct gccaaacac 60
acaacagctc tctcgagtag aacatctttg aaggcatgga gtgccgcggc tcccactgg 120
tggtcacacg ccaggggaag attgtcctgg aggacggcac cctgcattgn accgaangct 180
ctggacgcta cattcccccg aagcccttcc ctgattttkt ttacaagcgt atcaaggcaa 240
ggagcaggct ggctgagctg agaggggttc ctcgtggcct gtatgacgga cccgtgtgtg 300
aagtgtctgt gacgcccagg acagtcactc cagcctcctc ggccaagacg tctcctgcca 360
agcagcaggc cccacctgtc cggaacctgc accagtctgg attcagtttg tctggtgtgc 420
agattgatga caacattccc cgccgcacca cccagcgtat cgtggcgccc cccggtggcc 480
gtgccaacat caccagcctg ggctagagct cctgggctgt gccgtccact ggggactggg 540
gatgggacac ctgaggacat tctgagactt ctttcttctt tccttttttt ttttttgttt 600
ttttttttta agagcctgtg atagttactg tggagcagcc agttcatggg gtcccccttg 660
gggccccaca ccccgctctc caccaagagt tactgatttt gctcatccac ttcctacac 720
atctatgggt atcacacca agactacca ccaagctcat acagggaacc acaccaaca 780
cttagacatg cgaacaagca gccccagcg agggctcctc tcgccttcaa cctcctagt 840
tctgttagca tcttcttttt catgggggga ggaagataa agtgaattgc ccagagctgc 900
ctttttcttt tcttttttaa aatttttaaga agttttcttt gtggggctgg ggaggggccc 960
gggtcaggga gagtcttttt tttttttttt ttttaatact aaattggaac atttaattcc 1020
atattaatac aagggggttg aactggacat cctaattgat caattacgtc atcaccagc 1080
tgattccggg tggttggcaa actcatcgtg tctgtcctga gaggctccac aatgccacc 1140
cgatcgcca ttctgtagtc ttcagggtca gctgttgata aaggggcagg cttgcgttat 1200
tggcctagat tttgtgcag attaaatcct ttgaggattc tcttctcttt taccattttt 1260
ctgcgtgtgc tcaactctctc tttctctctc tagcttttta attcatgaat attttcgtgt 1320
```

```

ctgtctctct ctctctctgt gtttcctcca gcccttgtct cggagacggg gttttcctcc 1380
cttgccccat tatcttttca cctcccagg ctaccatttc atggtggtcg ttgggtccgc 1440
ctaaaaggatt tgagcgtttg ccattgcaag catagtgtcg tgcatcctg gtccatgtag 1500
gactgggtgct aaccacctgc catcatgagg atgtgtgcta gagtgtggga ccctggccaa 1560
gtgcaggaat gggccatgcc gtctcaccca cagtatcaca ygtggaaccg cagacagggc 1620
ccagaagctt tagaggtag aggtgcaga accggagaga ttttcctctg tgcagtgtc 1680
tctggctaaa gtcacgggtca aacctaaaca ccgagcctca ttaacccaag tgaaccaacc 1740
aaagtcacca gttcagaagt gctaagctaa taggagtctg acccgagggc ctgctgtctc 1800
ctggttaagt atcttttgag attctagaac acatgggagc tttttatatt cggggaaaaa 1860
ccgtattttt ttcttgtcca attatttcta aagacacact acatagaaag aggccctata 1920
aactcaaaaa gtcattggga aacttaaagt ctattctact ttgcaagagg agaaatgtgt 1980
tttatgaacg atagatcaca tcagaactcc tgtggggagg aaaccttata aattaaacac 2040
atggccccct tagagaccac aggcgatgtc tgtctccatc ctccctctc cttttctgtc 2100
acctttcccc ctagtgtggt cctttggacc taccctgtc cttgtgtact tgtgttgcac 2160
tgtattccaa acgtgtttac aggttctctt aagcaatgtt gtatttgac gcttttctga 2220
ataccaaatc tgctttttgt aaagcgtaaa aacatcacia agtaggtcat tccatcacca 2280
cccttgctc tctacacatt ttgccttttg ggatctggtt ggggttttgg gttttttgtt 2340
gttgtgtttt atttgttatt ttaaaggtaa attgcacttt taaaaaata attggttgac 2400
ttaatatatt tgcttttttt ctcacctgca cttagaggaa atttgaaca gttggaaaaa 2460
aacaattttt gtttcaattc taagaaacac ttgcagctct agtattcact tgagtcttcc 2520
tgtttttctt gtaccgggtc atggtaatth ttggtgtttt tggttgtttt cttaaaaaac 2580
aagttaaaac ctgacgattt ctgcaggctg tgtaagcatg ttacctgtt ggcttgcttt 2640
gtgtgtctgt taaatgaatg tcatatgtaa atgctaaaat aaatcgacag tgtctcagaa 2700
ctgaataact gcagtgtact gatgtcttaa aacagtgtag gayttaagaa tagatgggtt 2760
ttaatcctgg aaattgtgat tgtgacctat gagtggagga actttcagtt ctaaagctga 2820
taaagtgtgt agccagaaga gtactttttt ttttgtaacc actgtcttga tggcaaaata 2880
attatggtaa aaaacaagtc tcgtgtttat tattccttaa gaactctgtg ttatattacc 2940
atggaacgcc taataaagca aatgtggtt gtttcaaaaa aaaaaaaaaa aaaaaaaaaa 3000
aaaaaaaaaa aaaaaaaaaa aaccccgggg gggggcccn 3039

```

<210> 239

<211> 1992

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (12)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (13)

<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (29)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (87)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1989)  
<223> n equals a,t,g, or c

<400> 239  
nacactcctg annctcccta aatttaatna agctggccct ccaccgcggt ggcggccgct 60  
ctagaactag tggatcccc gggctgnagg aattcggcac gagcgcggtg ctgctgcgcc 120  
tgggcgatga gctggagatg atccggccca gcgtctaccg caacgtggcg cgtcagctgc 180  
acatctccct gcagtctgag cctgtggtga ccgatgcgtt cctggccgtg gctggccaca 240  
tcttctctgc aggcattcacg tggggcaagg tgggtgccct gtatgcggtg gccgcggggc 300  
tggccgtgga ctgtgtgagg caggcccagc ctgccatggt ccacgccctc gtggactgcc 360  
tgggggagtt cgtgcgcaag accctggcaa cctggctgcg gagacgcggc ggatggactg 420  
atgtcctcaa gtgtgtggtc agcacagacc ctggcctccg ctcccactgg ctggtggctg 480  
cactctgcag cttcggccgc ttctgaagg ctgccttctt cgtgctgctg ccagagagat 540  
gagctgcccc cctggcagtg gccgcagcct ggccctctgg ccaacgcagg aggccctcag 600  
caccgaaca catcttctc ctccccacc gagcctggag cactctaacc ctcgagacc 660  
ccctaagccc cgttctctccg cagaccagc ccctccggaa ggggtgagtg gggaggggct 720  
ttcctgagcc tggagctggg ctttggggca gcctgcgacc ctccccgctt gtgtcccttc 780  
tcctgtgatc tctgtgtttt cccttttctt tctggggcca ggaagtcagg gtcaactccc 840  
aggcctcaga tgcaggggcc cagaacacct gctctcacct gagccccagg tgaaggggccc 900  
cgggaacacc tgctctcacc tgagccccag gtgaaggggc ccgggaacac ctgctctcac 960  
ctgagcccca ggtgaagggg cccggaacac ctgctctcac ctgagcccca ggtgaagggg 1020  
cccgggaaca cctgctctca cctgagcccc aggtgaaggg gcccggaaca cctgctctca 1080  
cctgagcccc aggtgaaggg gcccggaaca cctgctctca cctgagcccc aggtgaaggg 1140  
gcccggaac acctctcacc tgaaccggg ggtcccatcc caggaagaag ggccatctca 1200  
ggacatgagt cctcaggggc cctgcacatt caatctgaag gtgaccttg cctggctgaa 1260  
gctggaagag ctgtggggac tcagcctgta aacagagcgt aaggttcaca tgcgtggtgc 1320  
ttaatccgtt tctggaggaa gagtatgaca ccacttgtg atggggctct tgtgcggtgg 1380  
ggaccggggc cggcgggctc caggccagca cacctaacc atggatgtgg aacctacggc 1440  
cgagaaggaa tgttgcatga gtcggatccc agtccattgt cagtggaggg tgaggggtgac 1500  
cccatctgct atttttgtgc tcatcctcat acaaccattt ggggatgtgc ctattagggc 1560  
tccgtaagaa ctcatagtgcc tgggaagccc agcccctcag gtgccccac acacagcctt 1620  
cccttgacgc ctacatttct aggcacatgt gaggcatctt tcctggagcc ccgagccagc 1680  
cctgtccctc ccagtgacg catggcactc aggagataca ggctggacat ggggcagtcg 1740  
ttctggggag gcctggccta gcagccacc acctgagccc tcccggccag gcttcgtgct 1800  
gggggtgggc atgtgccagg acaggagggg cccggcgga agccagcccc ggactcatcg 1860  
tgacattgag atcccaactg agggtagggg tggtaataaa cttctccaaa cgatgcgttg 1920  
tcattttaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980  
aaaaaaaaanc cc 1992

<210> 240

<211> 497  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (387)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (476)  
<223> n equals a,t,g, or c

<400> 240  
ggcagaactg tctgggacag acgctgcccg gatccctgcg gctgcctgca ctctggacca 60  
cgagctctga gagcagcagg ttgagggccg gtgggcagca gctcggaggc tccgcgaggt 120  
gcaggagacg caggcatggc cgggtgagctg actcctgagg aggaggccca gtacaaaaag 180  
gctttctccg cggttgacac ggatggaaac ggcacatca atgcccagga gctgggcgcg 240  
gcgctgaagg ccacgggcaa gaacctctcg gaggccagc taaggaaact catctccgag 300  
gttgacrgcg acggcgacgg cgaaatcagc ttccaggagt tcctgacggc ggcrargaag 360  
gccagggccg gcctggagga cctgcangtc gccttcgcg ccttcgacca ggatggcgac 420  
ggccacatca ccgtggacga gctcaggcgg gccatkgcgg ggytggggma ccttcnagag 480  
attgaccatt ttggagc 497

<210> 241  
<211> 316  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (133)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (311)  
<223> n equals a,t,g, or c

<400> 241  
atcgggcagc ccacacaagc ggcaaaccag aatggcactg gaaatggagc cgagaggta 60  
cgcgatgagg atcattccag gcgcgattgc actcataagc tggtccgttt tgaaaattcg 120  
tgttcaacga tgnaatctgt ggataatacg cacatttcgc cggaagtggg atccggttag 180  
ccaraaagca ggcaggacgt gatggatatt gtatttatag agcaactttc ggtaatcacc 240  
actattggtg tttagcactg ggrrcaacya tcgaacagaa gttagtgttc gatatcgaaa 300  
tggcgtgggg ntaacc 316

<210> 242  
<211> 829  
<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (14)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (47)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (793)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (809)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (814)

<223> n equals a,t,g, or c

<400> 242

ngnntttctt cggngggggg gaataagggg acacagctca cactatntta aggtacgcct 60  
gcaggtaccg gtcggaatt cccgggtcga cccacgcgtc cggaaagaaa agaagaaaag 120  
aaaaaaagat cttcaaaagg gcagatgggt agaaggcata acctctgagg gttaccatta 180  
ctattatgat ctatctcag gagcatctca gtgggagaaa cctgaaggat ttcaaggaga 240  
cttaaaaaag gtaattgaag catattaata gtgtttttgt tttattcttt acagtgattc 300  
gtttcttagg tttttgtaga gttttgctaa gcaactttat ttacaaatac tccactccct 360  
ccacccccaa actgtgtcct tttttttccc ataatgcttt tgtagaagg ctggatggag 420  
atgaaatagt gatatctggc tgggtgcagt ggctcatgcc tgtaatccca gcactttggg 480



```

aggetgaggc atgtggatca caaggtcagg agttaaagac cagcctggcc aagatgggtga 540
aaccctatct ctctctaaaa ctacaaaaaa attagccagg cgcagtcgca gttgcctgta 600
atcccagcta ctcaggaggc tgagtcaggg gaatcactgg gacctggggc ggcagagggt 660
aacagtgagc cgagattgca ccaccgcact ccagcctgga taacaaagta agactccgtc 720
tcaaaaaaaaa aaaaaaaaaa agggcggccg ctctagagga tccctcgagg ggcccaagct 780
tacgcgtgca tknaacgtca taggggctng ggcntttacc tttcccgtc 829

```

<210> 243

<211> 838

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (32)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (51)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (822)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (832)

<223> n equals a,t,g, or c

<400> 243

```

taaaccggaa gtgccaata ataatttaaa anatgttaat ttttttggcc ncctaaattt 60
gccctttcca tccattaaaa atgtccaagt tccaagtgat atgtgcccct aatatccacc 120
ttggatgttg gtgggttttt gaatttttgg gtggttaatc cagttttatt ttgaaaagac 180
gtacttgaat agttacagca tatgtttgaa caggaagtag gaacatgcat acacgaagaa 240
atgctaacgg aaggatttgt tatgtttagg atcttccctt ggaaactaaa aatagaatat 300
taatgacatt actgtttgta gaatgacata tgcagatttt ctcataagca gtcatttgtt 360
ttgccagtaa tgtttgagag acatgtaagt tgaaaagttt gctaaattat aaagctcctt 420
taattcgttg gttttgattc tcttattctc ttgtcttttc taaatgttaa caaaatatat 480
cttaacagat tacatgaaat ttaggaatta tttaaaagtt accattagct ctaaaattaa 540
gattcggatg cttttattat agtaactgaa gctaataatg ttttatgttt tgattttttg 600
aaatttaatt gtagaagtca ctgccttctg agttttcaaa tagataacca cctttaatat 660
tacactgctt ataatactaa tgtttacaga tatgtttctg tttataacca tataatacat 720
tggctttgtc atattagttt tttttgcaag tagttatgta aaagagatag ataataaaat 780
attaaataac aaaaaaaaaa raaaargctc gagtaarggc anagtggcat gngccata 838

```

<210> 244

<211> 2853

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2665)

<223> n equals a,t,g, or c

<400> 244

```

ggcacagcaa cagctctggg accatctcag gccccgctgc cctccccctag gccacaggca 60
gccccgtgtc catcttcgtc tatgatgtga agcctggcgc ggaagagcag acccaggtgg 120
ccaaagctgc cttcaagcgc ttcaaaactc tacggcacc ccaatcctg gcttacatcg 180
atggactgga gacagaaaaa tgctccacg tcgtgacaga ggctgtgacc ccgttgggaa 240
tataacctcaa ggcgagagtg gaggtgtgtg gcctgaagga gctggagatc tcctgggggc 300
tacaccagat cgtgaaagcc ctcagcttcc tggccaacga ctgcagcctc atccacaaca 360
atgtctgcat ggccgccgtg ttcgtggacc gagctggcga gtggaagcctt gggggcctgg 420
actacatgta ttcggcccag ggcaacggtg ggggamctcc ccgcaaggga tccccgagct 480
tgagcagtat gaccccccg agttggctga cagcagtggc agagtgtgca gagagaagtg 540
gtcagcagac atgtggcgct tgggctgcct catttgggaa gtcttcaatg ggcccctacc 600
tcgggcagca gccctacgca accctgggaa gatcccaaa acgctgggtg cccattamtg 660
taagctggtg ggagcaaac ccaaggtgctg tcccaaccca gcccgttcc tgcagaactg 720
ccgggcacct ggtggcttca tgagcaaccg cttttagaa accaacctct tcctggagga 780
gattcagatc aaagagccag ccgagaagca aaaattcttc caggagctga gcaagagcct 840
ggacgcattc cctgaggatt tctgtcggca caagggtgctg cccagctgc tgaccgcctt 900
cgagttcggc aatgctgggg ccgttgtcct cacgcccctc ttcaaggtgg gcaagttcct 960
gagcgtgtag gagtatcagc agaagatcat ccctgtggtg gtcaagatgt tctcatccac 1020
tgaccgggccc atgcgcattc gcctcctgca gcagatggag cagttcatcc agtaccttga 1080
cgagccaaca gtcaacaccc agatcttccc ccagctcgta catggcttcc tggacaccaa 1140
ccctgccatc cgggagcaga cggtaagtc catgctgctc ctggcccaa agctgaacga 1200
ggccaacctc aatgtggagc tgatgaagca ctttgacgg ctacaggcca aggatgaaca 1260
gggccccatc cgctgcaaca ccacgtctg cctgggcaaa atcggctcct acctcagtgc 1320
tagaccaga cacaggggtc ttacctctgc cttcagccga gccactaggg acccgttgc 1380
accgtcccgg gttgcgggtg tcctgggctt tgctgccacc cacaacctct actcaatgaa 1440
cgactgtgcc cagaagatcc tgcctgtgct ctgcggtctc actgtagatc ctgagaaatc 1500
cgtgcgagac caggccttca aggcattcgg agcttcctgt ccaaattgga gtctgtgtcg 1560
gaggaccgga cccagctgga ggaagtggag aaggatgtcc atgcagcctc cagccctggc 1620
atgggaggag ccgcagctag ctgggcaggc tgggcccgtga ccggggtctc ctactcacc 1680
tccaagctga tccgttcgca cccaaccact gcccacacag aaaccaacat tcccaaaga 1740
cccacgcctg aaggagtctc tgcccagcc cccaccctg ttctgccac ccctacaacc 1800
tcaggccact gggagacgca ggaggaggac aaggacacag caggagacag cagcactgct 1860
gacagatggg acgacgaaga ctggggcagc ctggagcagg aggccgagtc tgtgctggcc 1920
cagcaggacg actggagcac cgggggcca gtgagccgtg ctatgcaggt cagcaactcc 1980
gaccacaaat cctccaaatc cccagagtcc gactggagca gctgggaagc tgagggtctc 2040
tggaacagg gctggcagga gccaagctcc caggagccac ctctgacgg tacacggctg 2100
gccagcgagt ataactggg tggcccagag tccagcgaca agggcgaccc ctctgctacc 2160
ctgtctgcac gtcccagcac ccagccgagg ccagactctt ggggtgagga caactgggag 2220
ggcctcgaga ctgacagtgc acaggtcaag gctgagctgg cccggaagaa gcgcgaggag 2280
cgcgggcggg agatggaggc caaacgcgc gagagggaag tggccaaggg ccccatgaag 2340
ctggggagccc ggaagtggga ctgaaccgtg cggtggccc ttcccggctg cggagagccc 2400
gccccacaga tgattttatt gtacaaacca tgtagcccg gccgcccagc caggccatct 2460
cacgtgtaca taatcagagc cacaataaat tctatttcac accccttggt cggggctcag 2520
tctagcccct gggaggcggc tggggctctg cgccgccctc gcagcccgcg cccacgtcag 2580

```

```

acgtgaacat caatttgctt cgaaagccaa gggtaaagag gcacgatytg atttatcagt 2640
ttctaggaaa cacctctggg agganagcag gcagcgcccr ccggagacct tacaaccgcc 2700
cgctaaccgg ggaggggggc cggtaggggc gcctcgggty tcaaggcgcc gggaggggtct 2760
wgcgggccctg aaggtcctk ggtccgagcc acaagtcggg gcagaagtga ggccgagctc 2820
gcggaaatcc ctcaagtgat caccgaggtc tgg                                     2853

```

<210> 245

<211> 1197

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (218)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1193)

<223> n equals a,t,g, or c

<400> 245

```

gctcgtgccg cggcctgctt ctacctggct gagatcacgc tggccctggg ccatctccac 60
tcccagggca tcatctaccg ggacctcaag cccgagaaca tcatgctcag cagccagggc 120
cacatcaaac tgaccgactt trgactctgc aaggagtcta tccatgaggg cgccgtcact 180
cacaccttct gcggcaccat tgagtacatg gccctgnag attctggtgc gcagtggcca 240
caaccgggct gtggactggt ggagcctggg ggccctgatg tacgacatgc tactggatc 300
gcccgccttt accgcagaga accggaagaa aaccatggat aagatcatca ggggcaagct 360
ggcactgccc ccctacctca ccccagatgc ccgggacctt gtcaaaaagt ttctgaaacg 420
gaatcccagc cagcggattg ggggtggccc aggggatgct gctgatgtgc agagacatcc 480
ctttttccgg cacatgaatt gggacgacct tctggcctgg cgtgtggacc cccctttcag 540
gcccgtgtct cagtcagagg aggacgtgag ccagtttgat acccgcttca caggcagac 600
gcccgtggac agtcctgatg acacagccct cagcgagagt gccaaccagg ccttcctggg 660
cttcacatac gtggcgccgt ctgtcctgga cagcatcaag gagggttct ccttcagcc 720
caagctgcgc tcaccaggc gcctcaacag tagcccccg gccccgtca gccccctcaa 780
gttctcccct tttgaggggt ttcgggccag cccagcctg ccggagccca cggagctacc 840
tctacctcca ctctgcccac cgccgcccgc ctcgaccacc gcccctctcc ccatccgtcc 900
ccccctcagg accaagaagt ccaagagggg ccgtgggcgt ccagggcgct aggaagccgg 960
gtgggggtga gggtagccct tgagccctgt ccctgcggct gtgagagcag caggaccctg 1020
ggccagttcc agagacctgg ggggtgtgtc gggggtgggg tgtgagtgcg tatgaaagt 1080
tgtgtctgct ggggcagctg tgcccctgaa tcatgggcac ggaggccgcc cgccrmgccc 1140
cgcgctcaac tgctcccgtg gaagattaaa gggctgaatc atgaaaaaaa aaaaaa 1197

```

<210> 246

<211> 848

<212> DNA

<213> Homo sapiens

<400> 246

```

ggcacgagga gagagacctg gcggccgggc agcatggcgg ggctggagct cttgtcggac 60
cagggctacc gggtagcagg gcggcgcgcc ggggagctgc gcaagatcca ggcgcggatg 120

```

```

ggcgtgttcg cgcaggctga cggctcggcc tacattgagc agggcaacac caaggcactg 180
gctgtggtct acggcccgcg cgagatccgg ggtccccggg ctcgagccct gccggacagg 240
gccctagtga actgtcaata tagttcagcg accttcagca cagggtgagcg caagcracgg 300
ccacatgggg accgtaagtc ctgtgagatg ggctgcagc tccgccagac ttctgaagca 360
gccatcctca cacagctgca cccacgctcc cagattgata tctatgtgca ggtgctacag 420
gcagatggtg ggacctatgc agcttgtgtg aatgcagcca cgctggcagt gctggatgcc 480
gggataccca tgagagactt tgtgtgtgcg tgctcagctg gcttcgtgga cggcacagcc 540
ctggcggacc tcagccatgt ggaggaagca gctggtggcc cccagctggc cctggccctg 600
ctgccagcct caggacagat tgcgctgctt gagatggatg cccggctgca cgaggaccac 660
ctggagcggg tggtggaggc tgctgccag gctgcccag atgtgcacac cctcttagat 720
cgagtgttcc ggcagcatgt gcgtgaggcc tctatcttgc tgggggactg accaccagc 780
cacccatgtc cagaataaaa ccctcctctg cccamaaaaa aaaaaaaaaa aaaaaaaaaa 840
aaaaaaaaa

```

<210> 247

<211> 1336

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (26)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1336)

<223> n equals a,t,g, or c

<400> 247

```

ccccgcgggg acaaggcccg gacgngccg cgggccgcca gcgcccgcgc gtctcgcagc 60
aagagagggtg gagaagagcg agtacttgag aaagaagagg aagaagatga tgatgaagat 120
gaagatgaag aagatgatgt gtcagaggcg tctgaagtgc ccgagagtga ccgtcctgca 180
ggtgcccagc accaccagct taacggcgag cggggacctc agagtgccaa ggagagggtc 240
aaggagtgga cccctgcgag accgcaccag ggccaggatg aaggcggggg gccagccccg 300
ggcagcggca cccgccaggt gttctccatg gcagccatga acaaggaagg gggaacagct 360
tctkttgccg ccgggccaga ctccccgtcc cccgtgcctt tgcccccagg caaaccagcc 420
ctacctgggg ccgacgggac cccctttggc tgctctcccg ggcgcaaaga gaagccatct 480
gatcccgtcg agtggaccgt gatggatgtc gtcgaatatt ttactgaggc tggattcccg 540
gagcaggcga cagttttcca agagcaggaa attgatggca aatctttgct gctcatgcag 600
cgcacagatg tgctcaccgg cctgtccatc cgcctcgggc cagccctgaa aatctacgag 660
caccacatca aggtgcttca gcaaggccac tttgaggatg atgaccocga tggcttctta 720
ggctgagcgc ccagcctcac ccctgccccg gcccatcccg gcccctatct cacccaagat 780
ccccagagt ccaggagctg gacggggaca ccctcagccc tcataacaga ttccaaggag 840
agggcaccct cttgtcctta tctttgcccc ttgtgtctgt ctcacacaca tctgtctctc 900
agcagctcgg tgtggggagg ggattgctcc ttaaacccca ggtggtgac cctccccacc 960
cagtcacagga catttttaga aaaaaaaaaa gaaatgtggg gggctttctc tctccccaa 1020
atcctcttcc gttcagccag atgtttcctg tataaatgtt tggatctgcc tgtttatttt 1080
ggtgggtggt ctttctctcc tccccacca cccatgcccc ccttctcagt ctgcccctgg 1140
cttcagccc ctaggggact agctgggtg ggggttcctg ggcttttct ctctccctc 1200
tttctttct gttgattgtc gctccagctg gctgtattgc tttttaatat tgcaccgaag 1260

```

ktttttttaaa taaaatttta aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1320  
 aaaaaaaaaa aaaaan 1336

<210> 248

<211> 1076

<212> DNA

<213> Homo sapiens

<400> 248

gccggagaga gcagttctcc cgggcacctg tgtcagccct gcccttgcc cctaaccacc 60  
 tgggtaagtc acaggcgggtg gtgctgtggt tctgggggca gaggcccatg cctccaagga 120  
 tgtcgccatc gacatgatgg actctcggac cagccagcag ctgcagctca ttgacgagca 180  
 ggattcctac atccagagtc gggcagacac catgcagaac attgagtcga caattgttga 240  
 gttgggctcc atctttcagc agttggcaca catggttaag gaacaggagg aaaccattca 300  
 gaggatcgac gagaacgtgc taggagccca gctggacgtt gaggccgccc attcagagat 360  
 cctcaagtac ttccagtctg tcacctccaa ccggtggctc atgggtcaaaa tcttcctcat 420  
 cctcattgtc ttcttcatca tctttgtggt ctctccttgc tgaaccctct ctactctgag 480  
 gcactctgtt ggggttttggg accctcctgg gaaggcaagt ggccagtgcg gccactgagc 540  
 ctgtgcaggg tacttgggag aaaggccctg ttcccttgga actgctaaga atgaccactg 600  
 cccctgatcc cccaccctt gcctctggcc accctgtcct cccccacca ccctcaggcc 660  
 tatgaaacac acagggttct agatttgaac tctgctgtga agtgactgga agggagcaga 720  
 ggccagctgg gggccagtgg gggaggttgt ttccactagg agatttttat aaaccctctc 780  
 cagcctctcc caaaggaagc gttggcagca aaggagatg atgcccttac ccaccttctc 840  
 gtgagtgaag agaggaagca gccccaggga ccaattttcc caattgacct ctttcttctc 900  
 ctttcaccat gtgaggcagg gagccctgag cccttcagct gcctgcacaa cccctgacat 960  
 tggtctgtgg tgactcaatc tgccaaatgt gctgcagctc gttttctccc aattacagca 1020  
 agactgtcag cctcaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 1076

<210> 249

<211> 2425

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (52)

<223> n equals a,t,g, or c

<400> 249

ccgcagcagt gccatctcc tgaccagtgc cactgtgac caagcagtg gnagtgccca 60  
 tgccctccca atgtccagg ccctagctgt gaccgmtgtg cccccaactt ctggaacctc 120  
 accagtggcc atggttgcca gccttggtgc tgccacccaa gccgggccag aggccmwcct 180  
 gcaacgagtt cacaggcag tgccactgcs gtgccggctt tggaggggcg acttggtctg 240  
 agtgccaaga gctccactgg ggagaccctg ggttgagtg ccatgcctgt rattgtract 300  
 ctcgtggaat agatacacct cagtgtcacc gttcacagg tcaactgcagc tgccgcccag 360  
 ggtgtctggt gtgcgctgtg accagtgtgc ccgtggcttc tcaggaaatct ttctgcctg 420  
 ccattccctgc catgcatgct tcggggattg ggaccgagtg gtgcaggact tggcagcccc 480  
 tacacagcgc cttagagcagc gggcgagga gttgcaacag acgggtgtgc tgggtgcctt 540  
 tgagagcagc ttctggcaca tgcaggagaa gctgggcatt gtgcagggca tcgtaggtgc 600  
 ccgcaacacc tcagccgcct ccaactgcaca gcttgtggag gccacagagg agctgcggcg 660  
 tgaaattggg gaggccactg agcacctgac tcagctcgag gcagacctga cagatgtgca 720

```

agatgagaac ttcaatgcca accatgcact aagtggctctg gagcgagata ggcttgcaact 780
taatctcaca ctgcggcagc tcgaccagca tcttgacttg ctcaaacatt caaacttcct 840
gggtgcctat gacagcatcc ggcatgccc tagccagtct gcagaggcag aacgtcgtgc 900
caatacctca gccctggcag tacctagccc tgtgagcaac tcggcaagtg ctcggcatcg 960
gacagaggca ctgatggatg ctgagaagga ggacttcaac agcaaacaca tggccaacca 1020
gcgggcactt ggcaagctct ctgcccatac ccacaccctg agcctgacag acataaatga 1080
gctggtgtgt ggggcaccag gggatgcacc ctgtgtctaca agcccttggt ggggtgccgg 1140
ctgtcgagat gaggatgggc agccgcgtg tgggggcctc agctgcaatg gggcagcggc 1200
tacagcagac ctagcactgg gccgggcccg gcacacacag gcagagctgc agcgggcact 1260
ggcagaagggt ggtagcatcc tcagcagagt ggctgagact cgtcggcagg caagcgaggc 1320
acagcagcgg gcccaggcag ccctggacaa ggctaagtct tccaggggac aggtggaaca 1380
ggccaaccag gaacttcaag aacttatcca gagtgtgaag gacttcctca accaggaggg 1440
ggctgacct gatagcattg aaatgggtggc cacacgggtg ctagagctct ccatcccagc 1500
ttcagctgag cagatccagc acctggcggg tgcgattgca gagcgagtcc ggagcctggc 1560
agatgtggat gcgatcctgg cacgtactgt aggagatgtg cgtcgtgccg agcagctact 1620
gcaggatgca cggcgggcaa ggagctgggc tgaggatgag aaacagaagg cagagacagt 1680
acaggcagca ctggaggagg cccagcgggc acagggtatt gcccaggggtg ccatccgggg 1740
ggcagtggtc gacacacggg acacagagca gaccctgtac caggtacagg agaggatggc 1800
aggtgcagag cgggcactga gctctgcagg tgaaagggtc cggcagttgg atgctctcct 1860
ggaggctctg aaattgaaac gggcaggaaa tagtctggca gcctctacag cagaagaaac 1920
ggcaggcagt gcccagggtc gtgcccagga ggctgagcag ctgctacgcg gtcctctggg 1980
tgatcagtac cagacggtga aggccctagc tgagcgcaag gcccaagggtg tgctggctgc 2040
acaggcaagg gcagaacaac tgcgggatga ggctcgggac ctggtgcaag ccgctcagga 2100
caagctgcag cggctacagg aattggaagg cacctatgag gaaaatgagc gggcactgga 2160
gagtaaggca gcccagttgg acgggttgga ggccaggatg cgcagcgtgc ttcaagccat 2220
caacttgag gtgcagatct acaacacctg ccagtgacct ctgccaagg cctaccccag 2280
ttcctagcac tgccccacat gcatgtctgc ctatgcactg aagagctctt kgcccgcagg 2340
gcccccaata aaccagtgtg aacccccaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2400
aaaaaaaaa aaaaaagaaa aaaaaa 2425

```

<210> 250

<211> 1408

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (252)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1387)

<223> n equals a,t,g, or c

<400> 250

```

acggggctgt gcggagcagc tgtgcagagc tgcaggcgcg cgtcatggct gctttgagac 60
agccccagggt cgcggagtgc tggccgaggc cgggcgagcc ttccgggagg agttcggggc 120
cgagcccagag ctggccgtgt cagcgccggg ccgcgtgcaa cctcatcggg gaacacacgg 180
actacaacca gggcctggtg ctgcctatgg ctctggagct catgacggtg ctggtgggca 240
gccccgcgaa gnatgggctg gtgtctctcc tcaccacctc tgagggtgcc gatgagcccc 300

```

agcggtgca gtttccactg cccacagccc agcgctcgct ggagcctggg actcctcggg 360  
gggccaacta tgtcaaggga gtgattcagt actaccagc tgccccctc cctggcttca 420  
gtgcagtggg ggtcagctca gtgcccctgg ggggtggcct gtccagctca gcatccttgg 480  
aagtggccac gtacaccttc ctccagcagc tctgtccaga ctcgggcaca atagctgccc 540  
gcgcccaggt gtgtcagcag gccgagcaca gcttcgcagg gatgccctgt ggcatcatgg 600  
accagttcat ctcaattatg ggacagaaag gccacgcgct gtcattgac tgcaggtcct 660  
tggagaccag cctgggtcca ctctcggacc ccaagctggc cgtgctcatc accaactcta 720  
atgtccgcca ctccctggcc tccagcgagt accctgtgcg gcggcgccaa tgtgaagaag 780  
tggcccgggc gctgggcaag gaaagcctcc gggagggtaca actggaagag ctaggaggctg 840  
ccagggacct ggtgagcaaa gagggcttcc ggcgggcccg gcacgtggtg ggggagattc 900  
ggcgcacggc ccaggcagcg gccgccctga gacgtggcga ctacagagcc tttggccgcc 960  
tcatggtgga gagccaccgc tcaactcagag acgactatga ggtgagctgc ccagagctgg 1020  
accagctggg ggaggctgcg cttgctgtgc ctgggggtta tggcagccgc atgacgggcg 1080  
gtggcttcgg tggctgcacg gtgacactgc tggaggcctc cgctgctccc cacgccatgc 1140  
ggcacatcca ggagcactac ggcgggactg ccaccttcta cctctctcaa gcagccgatg 1200  
gagccaaggt gctgtgcttg tgaggcacc ccaggacagc acacggtgag ggtgcggggc 1260  
ctgcaggcca gtcccacggc tctgtgcccg gtgccatctt ccatatcccg gtgctcaata 1320  
aacttgtgcc tccaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1380  
aaaaaanaaa aagaaaaaaa aaaaaaaa 1408

<210> 251

<211> 494

<212> DNA

<213> Homo sapiens

<400> 251

gccggagccc acggtgggtca tggtgccag agcrtctgc atgctggggc tggctcctggc 60  
cttgtgtgcc tccagctctg ctgaggagta cgtgggcctg tctgcaaacc agtgtgccgt 120  
gccagccaag gacagggtgg actgaggcta ccccatgtc accccaagg agtgcaacaa 180  
ccggggctgc tgctttgact ccaggatccc tggagtgcct tgggtgttca agcccctgca 240  
ggaagcagaa tgcaccttct gaggcacctc cagctgcccc cggccggggg atgcgaggct 300  
cggagcaccc ttgccggct gtgattgctg ccaggcactg ttcattctag cttttctgtc 360  
cctttgtctc cggcaagcgc ttctgtgaa agttcatatc tggagcctga tgtcttaacg 420  
aataaaggct ccatgctcca ccgaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480  
aaaaaaaaaa aagg 494

<210> 252

<211> 2491

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (16)

<223> n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (2457)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 252

```
ggcggnggcg cccggnccctc gcccggccacg cagccgcccac cgctgctgcc gccctcggcc 60
acgggtcccg acgcgacagt gggcggggcca gcgccgaccc cgctgctgcc cccctcggcc 120
acagcctcgg tcaagatgga gccagagaac aagtacctgc ccgaactcat ggccgagaag 180
gactcgctcg acccgctcctt cactcacgcc atgcagctgc tgacggcaga aattgagaag 240
attcagaaaag gagactcaaa aaaggatgat gaggagaatt acttggattt attttctcat 300
aagaacatga aactgaaaga gcgagtgcgt atacctgtca agcagtatcc caagttcaat 360
tttgtgggga agattcttgg accacaaggg aatacaatca aaagactgca ggaagagact 420
ggtgcaaaaga tctctgtatt gggaaagggc tcaatgagag acaaagccaa ggaggaagag 480
ctgcgcaaaag gtggagaccc caaatatgcc cacttgaata tggatctgca tgtcttcatt 540
gaagtctttg gaccccatg tgaggcttat gctcttatgg cccatgccat ggaggaagtc 600
aagaaatttc tagtaccgga tatgatggat gatattctgtc aggagcaatt tctagagctg 660
tcctacttga atggagtacc tgaaccctct cgtggacgtg ggggtgccagt gagaggccgg 720
ggagctgcac ctctccacc acctgttccc aggggcccgtg gtgttgacc acctcggggg 780
gctttgttac gtggtacacc agtaagggga gccatcacca gaggtgccac tgtgactcga 840
ggcgtgccac cccacctac tgtgagggt gctccagcac caagagcacg gacagcgggc 900
atccagagga tacccttgcc tccacctcct gcaccagaaa catatgaaga atatggatat 960
gatgatacat acgcagaaca aagttacgaa ggctacgaag gctattacag ccagagtcaa 1020
ggggactcag aatattatga ctatggacat ggggaggttc aagattctta tgaagcttat 1080
ggccaggacg actggaatgg gaccaggccg tcgctgaagg cccctcctgc taggccagt 1140
aagggagcat acagagagca cccatatgga cgttattaaa aacaaacatg aggggaaaat 1200
atcagttagt agcaaaagtg ttactgattt cttgtatctc ccaggattcc tgttgcttta 1260
cccacaacag acaagtaatt gtctaagtgt tttcttcgt ggtcccttc ttctccccc 1320
cttattccat tcttaactct gcattctggc ttctgtatgt agtattttta aatgagttta 1380
aatagattta ggaatattga attaatTTTT taagtgtgta gatgcttttt tctttgttgt 1440
ttaaatataa acagaagtg accttttata ataaaaaaaa gaagttgagt aaaaaaaaaa 1500
aacacacaaa cctgttagtt tcaaaaatga cattgcttgc ttaaagggtc tgaagtaaag 1560
gcttgttaaag tttctcttag ttttgatttg aggcacccc taaagttgta gtgcagaat 1620
cccaaaactag gctacatttc aaaattcagg gctgtttaag atttaaaatc acaaacatta 1680
acggcagtag gcaccacat gtaaaagtga gctcagacgt ctctaaaaaa tgtttccttt 1740
ataaaagcac atggcggttg aatcttaagg ttaaatttta atatgaaaga tcctcatgaa 1800
ttaaatagtt gatgcaattt ttaacgttaa ttgatataaa aaaaaaaaca acaaaattag 1860
gcttgtaaaa ctgacttttt cattacgtgg gttttgaaat ctagccccag acatactgtg 1920
ttgagagata cttagaggga gggagtaggt tttgaagagg ttgatggtgg tggggaggga 1980
aggcctcctg aattgagttt gatgcagagc tttttagcca tgaagaatct ttcagtcata 2040
gtactaataa ttaaattttc agtattttta aagacaaagt attttgtcca tttgagattc 2100
tgactccat gaaaagttca cttggacgct gggggccaaa gctgttgatt ttcttaagtt 2160
gacggttgtc aatatatcga actgttccca agttagtcaa gtatgtctca acactagcat 2220
gatataaaaa gggacactgc agctgaatga aaaaggaatc aaaatccact ttgtacataa 2280
gttaaagtcc taattggatt tgtaccgtcc tcccattttg ttctcggag attaaatgct 2340
acatgtgtaa gtctgcctaa ataggtagct taaacttatg tcaaaatgtc tgcagcagtt 2400
tgtcaataaa gtttagtcct tttttaatca aaaaaaaaaa aaaaaaaaaa aggcggncgc 2460
tctagaggat ccaagcttac gaccccgcca t 2491
```

&lt;210&gt; 253

&lt;211&gt; 1125



&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 253

```

ttcgttttagg tccgctggaa attatgtcct ccgtcggttt tccgcagttt ttccaccaag 60
cgagatattt ttgggagtta ttccctaaat aactgcatta tatgctcctt tcatgacgaa 120
attgctgccc tggagaagac tggaggaaac tcgaggaaga gggagaagcc gacaagtgct 180
cgacgggcta ggaactgtcc tgcttgggtg ttagcgtttc ccgycgggcc agtaaggctg 240
agtgacccgg cgtgctacta ggagaaggac gtacggctct gctagtagag gaatatgtcg 300
agtttctcta gggcgcccca gcaatgggcc acttttgcta gaatatggta tctcttagat 360
gggaaaatgc agccacctgg caaacttgct gctatggcat ctataagact tcagggatta 420
cataaacctg tgtaccatgc actgagtgc tgtggggatc atgttggtat aatgaacaca 480
agacacattg cattttctgg aaacaaatgg gaacaaaaag tatactcttc gcatactggc 540
taccagggtg gatttagaca agtaacagct gctcagcttc acctgagggg tccagtggca 600
attgtaaaac tagctattta tggcatgctg ccaaaaaacc ttcacagaag aacaatgatg 660
gaaagggtgc atctttttcc agatgagtat attccagaag atattcttaa gaatttagta 720
gaggagcttc ctcaaccacg aaaaatacct aaacgtctag atgagtacac acaagaagaa 780
atagacgcct tcccaagatt gtggactcca cctgaagatt atcggctata agagaataag 840
aattgcagaa aataacagtg aagtgattga aactttcttc tgatgagttt ctctaacct 900
caggatggag taaacaact gctacagtc agcacctgtt ttatgtgccg aatcactgtg 960
gggaaaggtc aggaagggtg agtccttcaa taggaaattg taattaaaat ataattttat 1020
agaaccattt ttatgtaatc tgatttgaat gttatagttg ataataataa aatcacttac 1080
ttggttgact atttagtggt gcatttaatg ataaaaaaca gaccc 1125

```

&lt;210&gt; 254

&lt;211&gt; 1409

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 254

```

cactttgtct tttcttaagt aattatggta tatataaggc gttgggaaaa aacattttat 60
aatgaaagta tgtagggagt caaatgctta ctgtaaatgc ataagagacg ttaaaaaata 120
cactgcactt tcaggaatgt ttgcttatgg tcttgattag aaagaaacag ttgtctatgc 180
tctgcaatgg tcaatgatga attactaatg ccttattttc taggcatata ataatagttt 240
agagaatgta gaccagataa atttgtttac tgttttaaga aaactaccag tttacttaca 300
gaagattctt ttttccaaac agtaggtttc atccaagacc atttgaagaa ctgcaaactc 360
tttctcttag aaaagaaaaga gggcagccta aaataaacgc aaaatttgct tatactccat 420
cacattcaga tgtcttggtt gtgacttatt accagtgtgg cagagaaccc aagttacatt 480
ttagatcaaa atattcttta ttaggtattt gttaaaaggc tagagcctac aagttgctct 540
tccatgcgtt ggtcaggggg ccctgaaaac actggtaata ttaagagtct ttctcagggt 600
aacttaatgt tttcttaatg aacartgttt ccagctacaa attcttycaa taaattgtct 660
tcctttttga aaagtactct catagaagaa atttagcaat ttctcgttga ctgactcagt 720
ctattttaag tattcagaaa agattttgat ccccatagag ttaatgctct gccttgaaaa 780
ttatttttct ggatccttgt tagtgataac atttttttct tactgaaggt cagaggatag 840
gaaacaagta tttctcttct ggtatacatg taatgtattc tgtaaaaaag tattcatatt 900
ggcaatttta gttaggcata atattgtggt tgtaattttt aaaacttagt gttttgtctg 960
attaaagcag gcactgatca gggatatctc taagaggtaa ttcacttctt attcctttcc 1020
aataattatt acattctaaa ttttcatcta tgagaaataa caaacaagaa gggaatagaa 1080
ttaaattggg gtataatcta atcttcattg tttaaatggt ttgccttctc accattgaag 1140
ccatttttta tagcctcaga aagaggaaat aatgcctcca ccattttcta cctggtgact 1200
tgaaaattga acttttaagt taggaagaag ttagagtcag ggaacttgta taccactatc 1260

```

```
tatgcagcat tgttatagtc tgattatttc tgtgttttga atatgatttt cctaattgctc 1320
taaataaaat tttgttaaaa attaattttt tatttaataga tgtgcaaata ttgaatatatt 1380
tagtatattt attaaaagtg gtagtcatt 1409
```

<210> 255

<211> 490

<212> DNA

<213> Homo sapiens

<400> 255

```
accacgcgct ccgcctctct gtcgtggcgc ggcttcccgc ggtcttctct gcaaattgggc 60
tccgtggcct agcgcccccg tccccgccac ccgtgatcgt gcgccgaggc ccgcgagggg 120
tcgccgcca ggccgcctgg gttccacttc cagcaacagc tcctgcagca gtaccgagtg 180
ccccggggaa gccattcccc acccccagg tctccccaag gctgaccgg gtcattgggtg 240
ggccagcttc ttttccggga agtccaccct cccgttcatt gccacgggtg tggagtccgc 300
agagcactcg gaacctcccc aggcctccag cagcatgamc gcctgtggcc tggctcggga 360
agccccgagg aagcagcccg gcggtcagtc cagcamagcc agcgctgggc ccccgctctg 420
aactgagcgg ttaacaacaa gcccgaagcc tkcggaagcg ctagtycaac agagccctcc 480
gggccccttg 490
```

<210> 256

<211> 1233

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (45)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (602)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (931)

<223> n equals a,t,g, or c

<400> 256

```
ggcagagggt ggctcggggc tatgagaacg tgcccattcc ctgtntcacg gtgtggatgg 60
ggagccctgc cctgaggatt acaagtacat ctgagagaac tgcgagacgt ccaccatgaa 120
catcgatcgc aacatcacc acctgcagca ctgcacgttt gtggacgact gctctagctc 180
caactgcctg tgcggccast tcagcatccg gtgctggtat gacaaggatg ggcgattgct 240
ccaggaattt aacaagattg agcctccgct gattttcgag tgtaaccagg cgtgctcatg 300
ctggagaaaac tgcaagaacc gggctcgtaca gagtggcatc aagggtgcgc tacagctcta 360
ccgaacagcc aagatgggct ggggggtccg cgccctgcag accatcccac aggggacctt 420
catctgcgag tatgtcgggg agctgatctc tgatgctgag gctgatgtga gagaggatga 480
ttcttacctc ttcgacttag acaacaagga tggagagggt tactgcatag atgcccgtaa 540
ctatggcaac atcagccgct tcatcaacca cctgtgtgac cccaacatca ttcccgtccg 600
```

```

gntcttcatg ctgcaccaag acctgcgatt tccacgcata gccttcttca gttcccgaga 660
catccggact ggggaggagc tagggtttga ctatggcgac cgcttctggg acatcaaaaag 720
caaatatttc acctgccaat gtggctctga gaagtgcgaag cactcagccg aagccattgc 780
cctggagcag agccgtctgg cccgcctgga cccacaccct gagctgctgc ccgagctcgg 840
ctccctgccc cctgtcaaca catgagaacg gaccacaccc tctytcccca gcatggatgg 900
ccacagctca gccgcctcct ctgccaccag ntgctcgag cccatgcctg ggggtgctgc 960
catcttctct cccaccacc ctttcacaca ttctgacca gagatcccag ccaggccctg 1020
gaggtctgac agccctccc tcccagagct ggttctctcc tgggagggca acttcagggc 1080
tggccacccc ccgtgttccc catcctcagt tgaagtttga tgaattgaag tcgggcctct 1140
atgccaactg gttccttttg ttctcaataa atgttgggtt tggtaaaaaa aaaaaaaaaa 1200
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aac                                     1233

```

<210> 257

<211> 2404

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2372)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2385)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2395)

<223> n equals a,t,g, or c

<400> 257

```

cggacggtgg gacgggsaag tgggggtgaa aagcgccccg acctgcttgc ggtgtagtgg 60
gcggaccgcg cggctggagg tgtgaggatc cgaaccagc ggtggggggg ggaggcggct 120
cctgcgatcg aaggggactt gagactcacc ggccgcacgc catgagggcc ctgtgggtgc 180
tgggcctctg ctgctcctg ctgaccttcg ggtcggtcag agctgacgat gaagttgatg 240
tggtatgtac agtagaagag gatctgggta aaagtagaga aggatcaagg acggatgatg 300
aagtagtaca gagagaggaa gaagctattc agttggatgg attaaatgca tcacaaataa 360
gagaacttag agagaagtcg gaaaagtttg ccttccaagc cgaagttaac agaattgatg 420
aacttatcat caattcattg tataaaaata aagagatttt cctgagagaa ctgatttcaa 480
atgcttctga tgctttagat aagataaggc taatatcact gactgatgaa aatgctcttt 540
ctggaaatga ggaactaaca gtcaaaatta agtgtgataa ggagaagaac ctgctgcatg 600
tcacagacac cgggttagga atgaccagag aagagttggg taaaacctt ggtaccatag 660
ccaaatctgg gacaagcgag tttttaaaca aaatgactga agcacaggaa gatggccagt 720
caacttctga attgattggc cagtttgggt tcggtttcta ttccgccttc cttgtagcag 780
ataaggttat tgtcacttca aaacacaaca acgataccca gcacatctgg gagtctgact 840
ccaatgaatt ttctgtaatt gctgacccaa gaggaacac tctaggacgg ggaacgacaa 900
ttacccttgt cttaaaagaa gaagcatctg attaccttga attggataca attaaaaatc 960
tcgtcaaaaa atattcacag ttcataaact ttcctattta tgtatggagc agcaagactg 1020
aaactgttga ggagcccatg gaggaagaag aagcagccaa agaagagaaa gaagaatctg 1080

```

```

atgatgaagc tgcagtagag gaagaagaag aagaaaagaa accaaagact aaaaaagttg 1140
aagaaacact ctaggacggg gaacgacaat tacccttgtc ttaaaagaag aagcatctga 1200
ttaccttgaa ttggatacaa ttaaaaatct cgtcaaaaaa tattcacagt tcataaactt 1260
tcctatttat gtatggagca gcaagactga aactgttgag gagcccatgg aggaagaaga 1320
agcagccaaa gaagagaaaag aagaatctga tgatgaagct gcagtagagg aagaagaaga 1380
agaaaagaaa ccaaagacta aaaaagttga aaaaactgtc tgggactggg aacttatgaa 1440
tgatatcaaa ccaatatggc agagaccatc aaaagaagta gaagaagatg aatacaaagc 1500
tttctacaaa tcattttcaa aggaaagtga tgaccccatg gcttatattc actttactgc 1560
tgaaggggaa gttaccttca aatcaatttt atttgtaccc acatctgctc cacgtggtct 1620
gtttgacgaa tatggatcta aaaagagcga ttacattaag ctctatgtgc gccgtgtatt 1680
catcacagac gacttccatg atatgatgcc taaatacctc aattttgtca aggggtgtgt 1740
ggactcagat gatctcccct tgaatgtttc ccgcgagact cttcagcaac ataaactgct 1800
taaggtgatt aggaagaagc ttgttcgtaa aacgctggac atgatcaaga agattgctga 1860
tgataaatac aatgatactt tttggaaaga atttggtacc aacatcaagc ttggtgtgat 1920
tgaagaccac tcgaatcgaa cacgtcttgc taaacttctt aggttccagt cttctcatca 1980
tccaactgac attactagcc tagaccagta tgtggaaaga atgaaggaaa aacaagacaa 2040
aatctacttc atggctgggt ccagcagaaa agaggctgaa tcttctccat ttggtgagcg 2100
acttctgaaa aagggtctatg aagttattta cctcacagaa cctgtggatg aatactgtat 2160
tcaggccctt cccgaatttg atgggaagag gttccagaat gttgccaagg aaggagtga 2220
gttcgatgaa agtgagaaaa ctaaggagag tcgtgaagca gttgagaaag aatttgagcc 2280
tctgctgaat tggatgaaag ataaagccct taaggcmag rtactgtggg aaattttacc 2340
aatttgtggg aaatattagt gtccggcatt tnaggggaaa gtttnttttt ggggnaacca 2400
aatt 2404

```

<210> 258

<211> 2092

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (27)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (31)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (60)

<223> n equals a,t,g, or c

<220>

<221> misc feature

&lt;222&gt; (2069)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (2071)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 258

```
tatncaacaa ctaaaacgac tcactanagg naaaagcagg aacgcctgca ggaaaccggn 60
ccggaattcc cgggtcgacc cacgcgtccg ctgccgctcc ctttgccgcc gccttagccc 120
gggacccgaa cccagcctct cccctacccc aacaccggcc cgggctccac cgaggccccg 180
gtcccccagc ccgtctcgcc gccgccatgg cggaccctaa atacgccgac cttcccgga 240
ttgccaggaa tgagccagat gtttatgaaa ctacgcacct acctgaggat gatcaagcgg 300
agttcgatgc ggaggagctg acaagcacia gtgtggaaca catcattgtc aatcctaattg 360
ctgcctatga caagtccaag gacaagagag tggggacaaa gggacttgat ttctcagatc 420
gtattggaia aaccaagagg acaggatatg aatctggaga atatgagatg cttggagagg 480
gtctgggagt gaaggagaca ccccagcaaa agtaccagcg cctactgcat gaggtccaag 540
agctgacaac tgaagttgaa aaaatcaaga cgacagtga ggaagtcagcc acagaggaga 600
agctgacccc tgtgttgctg gctaaacagc tggcagccct gaagcagcag ctggttgctt 660
ccacactgga gaagctgctg ggaccagatg ctgcaatcaa ccttaccgac cccgatggcg 720
ccctggctaa ggcgcctacta ctgcagctgg aagcaacaaa gaacagcaaa ggggatcag 780
ggggaaaaac cactgggacc ccccagata gcagccttgt cacttatgaa ctacattctc 840
ggcctgagca ggacaagttc tctcaagctg ccaaagtcgc agaacttgaa aagcgctga 900
cagagctgga gacagctgta cgttgtgatc aggatgctca gaatccccct tctgcaggtc 960
tacagggagc ctgtctcatg gagactgtag agctgttgca agcaaagggt agcgccctag 1020
accttgcatg tttggatcaa gtggaggctc ggctacagag tgcctctgga aaggtgaacg 1080
agattgccaa gcataaagcc tctgtagaag atgcagatac acaaagcaag gtgcaccagc 1140
tatatgaiaa tatacagcgc tggagcccca ttgcctccac cctccctgag ctggtgcaga 1200
gacttgctac catcaagcag ctgcacagagc aagccatgca gtttggtcag ctctgacac 1260
acttgatata caccagcagc atgattgcta attccttgaa ggacaatacc accctcttga 1320
cccagggtga gacaacatg cgtgaaaacc tggccacagt tgaggggaac tttgccagca 1380
ttgatgaacg gatgaagaag ctgggaaagt gagcacattt gggagctgga gaacaggggt 1440
tatccctacc cctgtgaact ctgttaacag cttacatagg gtttccccct tactataact 1500
ctagcatccc catcccattt gacactgggg gcaagggttc ttcttgcatg tggggtttat 1560
accctcccc tgatgaatac agagtggtag ctagggttg gttatcatca gaaggtggtc 1620
tcccctcagg cctgggggat aaggacgtgg gccagccac atgccaactc atgtccaata 1680
ctgctttgcc tgggtgtggg aaggattggg tcttgtcccc caacacagct tctgtggctg 1740
actgtaatac tgtacaactg tttctgacca ttaaagtctg ttgtactctg tgtggcctct 1800
gctgtgtttc ctggggagga agcagcacta ggatatagat attcattcgt cataacaggc 1860
aatctaagcc actctatact acaagagatg gatttaaatt gtaacctgtt cttaccaaaag 1920
aactaaataa aaaatgagta cagagccaga gccagagttt caaaatattc tcatctgtta 1980
aattaagagt gtctcccata gaaaagcagt ggaggcccca cagggcaagt acaaaacaga 2040
attaaaactc aaaaaaaaaa aaaaaaaanc ncaagggggg gcccggtccc ca 2092
```

&lt;210&gt; 259

&lt;211&gt; 387

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

<221> misc feature

<222> (377)

<223> n equals a,t,g, or c

<400> 259

```
aattcggcac gaggttcat tctctgacct ttctctctcc tcatttcggt gcatgtcctt 60
tctgcagctg cctttcagca caggtggctg cccccaggg ccaccgcttc tttcttgatc 120
ctctttcctt aacagtgact tgggcttgag tctggcaagg aaccttgctt ttagcttcac 180
caccaaggag agagaccaa agcctctgat ttttaatttc cataaaatgt tagaagtata 240
tatatacata tatatatattc tttaaatttt tgagtctttg atatgtctaa aatcattcct 300
ctgcctgaag cctkagtga ccatgarga actgtgttca ttaagtgtta ttaatgttga 360
actgaaaaaa aaaaacnggg ggggccg                                     387
```

<210> 260

<211> 3712

<212> DNA

<213> Homo sapiens

<400> 260

```
tatccccgac gaccggatcc tgaggaggca gctgcggtgg cagctgctga gttctcggtg 60
aaggtatttc atttctcctg tccccctccc tccccacccc atctattaat attattcttt 120
tgaagattct tcgttgtaaa gccgccaaag tggagagtgc gattgcagaa gggggtgctt 180
ctcgtttcag tgcttcttcg gccggaggag gaagttagggg tgcacctcag cactatccca 240
agactgctgg caacagcgag ttcttgggga aaacccagg gcaaacgct cagaaatgga 300
ttcctgcacg aagcactaga cgagatgaca actccgcagc aaacaactcc gcaaacgaaa 360
aagaacgaca tgatgcaatc ttcaggaaaag taagaggcat actaaataag cttactcctg 420
aaaagtttga caagctatgc cttgagctcc tcaatgtggg tgtagagtct aaactcatcc 480
ttaaaggggt catactgctg attgtggaca aagccctaga agagccaaaag tatagctcac 540
tgtatgctca gctatgtctg cgattggcag aagatgcacc aaactttgat ggcccagcag 600
cagagggtca accaggacag aagcaaaagca ccacattcag acgcctccta atttccaaat 660
tacaagatga atttgaaaac cgaactagaa atggtgatgt ctatgataag cgtgaaaatc 720
ccctcctccc cgaggaggag gaacagagag ccattgctaa gatcaagatg ttgggaaaaca 780
tcaaattcat tggagagctt ggcaagcttg atcttattca cgaatctatc cttcataagt 840
gcatacaaac acttttgaa aagaagaaga gagtccaact caaagatatg ggagaggatt 900
tgagtgacct ctgtcagata atgaggacag tgggacctag attagaccat gaacgagcca 960
agtccttaat ggatcagtac tttgcccga tgtgctcctt gatgttaagt aaggaattgc 1020
cagcaaggat tcgtttcctg ctgcaggata ccgtagagtt gcgagaacac cattgggttc 1080
ctcgcaaggc tttcttgac aatggaccaa agacgatcaa tcaaattcgt caagatgcag 1140
taaaagatct aggggtgttt attcctgctc ctatggctca agggatgaga agtgacttct 1200
ttctggaggg accgttcatg ccacccagga tgaaaatgga tagggaccca cttggaggac 1260
ttgctgatat gtttgacaaa atgccaggta gcggaattgg tactgggtcca ggagttatcc 1320
aggatagatt ttcaccacc atgggacgtc atcgttcaaa tcaactcttc aatggccatg 1380
ggggacacat catgcctccc acacaatcgc agtttgaga gatgggaggc aagtttatga 1440
aaagccaggg gctaagccag ctctaccata accagagtca gggactctta tcccagctgc 1500
aaggacagtc gaaggatatg ccacctcggt tttctaagaa aggacagctt aatgcagatg 1560
agattagcct gaggcctgct cagtcgttcc taatgaataa aaatcaagtg ccaaagcttc 1620
agccccagat aactatgatt cctcctagtg cacaaccacc acgcactcaa acaccacctc 1680
tgggacagac acctcagctt ggtctcaaaa ctaatccacc acttatccag gaaaagcctg 1740
ccaagaccag caaaaagcca ccaccgtcaa aggaagaact ccttaacta actgaaactg 1800
ttgtgactga atatctaaat agtggaatg caaatgaggc tgtcaatggt gtaagagaaa 1860
tgagggctcc taaacacttt ctctctgaga tgttaagcaa agtaatcatc ctgtcactag 1920
```

```

atagaagcga tgaagataaa gaaaaagcaa gttctttgat cagtttactc aaacaggaag 1980
ggatagccac aagtgacaac ttcattgcagg ctttcctgaa tgtattggac cagtgtccca 2040
aactggaggt tgacatccct ttggtgaaat cctatttagc acagtttgca gctcgtgcc 2100
tcatttcaga gctggtgagc atttcagaac tagctcaacc actagaaagt ggcacccatt 2160
ttctctctt cctactttgt cttcagcagt tagctaaatt acaagatcga gaatggtaa 2220
cagaactttt tcaacaaagc aaggtcaata tgcagaaaat gctcccagaa attgatcaga 2280
ataaggaccg catgttggag attttggag gaaagggaact gagtttctta tccctactcc 2340
tcaaattgga gaaggaactg ttgaagcaaa taaagttgga tccatcccct caaacatat 2400
ataaatggat taaagataac atctctccca aacttcatgt agataaagga tttgtgaaca 2460
tcttaatgac tagcttctta cagtacattt ctagtgaagt aaaccccccc agcgatgaaa 2520
cagattcatc ctctgctcct tccaaagaac agttagagca ggaaaaacaa ctactactat 2580
ctttcaagcc agtaatgcag aaatttcttc atgatcacgt tgatctacaa gtcagtgcgc 2640
tgtatgctct ccagggtgcac tgctataaca gcaacttccc aaaaggcatg ttacttcgct 2700
tttttgtagc cttctatgac atggaaatta ttgaagaaga agctttcttg gcttggaag 2760
aagatataac ccaagagttt ccgggaaaag gcaaggcttt gttccagggtg aatcagtggc 2820
taacctggtt agaaactgct gaagaagaag aatcagagga agaagctgac taaagaacca 2880
gccaaagcct taaattgtgc aaaacatact gttgctatga tgtaactgca tttgacctaa 2940
ccactgcgaa aattcattcc gctgtaatgt tttcacaata tttaaagcag aagcacgtca 3000
gttaggattt ccttctgcat aagggttttt ttagtgtaa tgtcttaatc atagtctacc 3060
atcaaatatt ttaggagtat ctttaatggt tagatagtat attagcagca tgcaataatt 3120
acatcataag ttctcaagca gaggcagctt attgcaagga ccttctttgc tgccagttat 3180
cataggctgt ttaagttag aaaactgaat agcaacactg aatactgtag aaatgcactt 3240
tgctcagtaa tacttgagtt gttgcaatat ttgattatcc atttggttgt tacagaaaaa 3300
ttcttaactg taattgatgg ttggtgccgt aatagtatat tgctgtatt tctacctcta 3360
gtaatgggct ttatgtgcta gattttaata tccttgagcc tgggcaagtg cacaagtctt 3420
tttaaagaa acatggttta cttgcacaaa actgatcagt tttgagagat cgttaatgcc 3480
cttgaagtgg tttttgtggg tgtgaaacaa atggtgagaa tttgaattgg tccctcctat 3540
tatagtattg aaattaagtc tacttaattt atcaagtcac gtccatgccc tgattttata 3600
tacttgtatc tatcaataaa cattgtgata cttgaaaaaa aaaaaaaaaa aaaaaaaaaa 3660
aaaaaaaaaa aaaaaaaaaa aaaaaaaagg aggaaaaaaa aaaaaaaaaa aa 3712

```

<210> 261

<211> 897

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (22)

<223> n equals a,t,g, or c

<400> 261

```

agagctggaa ggaggaggag angaaacctc accttcaggg caaaccaggg agacccttgt 60
ccccggccaa tgtccctgct ctgcctggcg agacgggtgac ctccccagtc aggtgcacc 120
ccgactacct ctccccggag gagatacaga ggcagctgca ggacatcgag aggcggctgg 180
acgccctgga gctccgcggc gtggagctgg agaagcgact gcgggcggcc gagggagatg 240
acgctgagga tagcctcatg gtggactggt tctggctcat tcacgagaag cagcttctgc 300
tgagacagga gtcagagctg atgtacaagt ccaaggccca gcgtctggag gagcagcagc 360
tgagacatga gggcgagctg cgccggctca tggccaagcc cgaggctctg aagtcaactgc 420
aggagcggcg gcgggagcag gagctgctgg agcartacgt gagcaccgtg aacgaccgca 480
rtgacatcgt ggactcgctk gacgaggacc ggctccsgga acaagaggag gatcagatgc 540

```

```

tgcgggacat gattgagaag ctgggcctcc agaggaagaa gtccaagttc cgcttgtcca 600
agatctgggtc accaaaaaagc aaaagcagcc cctcccagta gtagccagta gggccgtggg 660
ctcgggccggg acctggcatc cggacttgga ctcggggcca tgggcttggc ccggaccggg 720
aaccgggact tgtactcggg gccgtgggct cggcccgga cgggcattcg gacttggact 780
cggaagggc ctctgtccc tacaaggggc atgtggacag caggacctg cgctaccgtc 840
tgtgtgtctca ataaagaaac cgaccacatg gaaaaaaaaa aaamaaaaaa aaaaaaa 897

```

&lt;210&gt; 262

&lt;211&gt; 1905

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1266)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1791)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 262

```

gctgtgatag cgcgtgagga ggcagaggcc tctgggggtg gatcgcgggc cgtaagtggc 60
tgtggagctg ggggtcactgc gcgtggggac catggcctcg gagaagccgc tggcggcagt 120
cacttgtaca gcgccgttca acatcgcggt catcaagtac tggggcaagc gcgatgaaga 180
gctggttctg cccatcaact cctccctgag cgtcactctg caccaggacc agttaaaaac 240
caccacaaca gccgtcatca gcaaggactt caccgaggac cggatttggc tgaatggccg 300
ggaggaggat gtggggcagc cgmggctgca ggctgcctg cgggagatcc gctgcctggc 360
ccggaagcgg aggaactcac gggatgggga cccgctgccc tccagcctca gctgcaaggt 420
gcacgtggga tcgggtgaaca acttccccac ggctgcgggc ctggcctcct cagcggcggg 480
ctatgcctgc ctagcctaca ccctggcccc tgtctacggc gtggagagtg acctctcaga 540
agtggctcgc cggggctcag gcagcgccts ccggagcctg tatgggggct ttgtggagtg 600
gcagatggga gagcaggccg acgggaagga cagcatcgct cggcaagtgg cccccgagtc 660
aactggcct gaactccgcg tgctcatcct tgtggtgagc gctgagaaga agctgacagg 720
cagtaccgtg ggcattgcgg ccagtgtgga gaccagcccc ctgcttcggt tccgggccga 780
gtccgtggtg cccgcgcgca tggcggagat ggcccgctgc atccgggagc gagacttccc 840
cagcttcgcc cagctgacca tgaaggacag caaccagttc caccgacact gcctcgacac 900
cttccccgcc atctcttacc tcaatgccat ctccctggcg atcatccacc tggcgcaccg 960
cttcaacgcc caccacgggg acaccaaggt ggcgtacacc tttgacgcgg gcccgaatgc 1020
cgtgatcttc accctggacg aactgtggc tgagtttgtg gctgctgtgt ggcacggctt 1080
tccccaggc tcgaatggag acacgtttct gaaggggctg caggtgaggc cggccccctt 1140
ctcagctgag cttcaggctg cgctggccat ggagccgacc cccgggtggg tcaaatacat 1200
cattgtcact caggtggggc cagggcctca aatcctggat gaccctgcg cccacctcct 1260
gggtcntgac ggcctgccga agccagctgc ctgactgcct cagcagggac cgcattgccg 1320
ttggagaagg ggtggcctcg ccggagctag ggagcggatg tgggtggctg gccggactcc 1380
tgggacatgt ggggtgtggc ttgaccccg gcccatggg agcttgctgt ggggcagtgc 1440
agggagtcct gcggccgccc aggtgtcagg agaggtcccc gccgagtgt tcagctgccc 1500
taagctgcac cagcgttttg ccaagatggg atggggaggg ggtatgagaa ctggcagagc 1560
ctcgggtcag cagggtgtaa gggttttct accccagctc tggctatgcc cagttctctg 1620
agaaaggagc tcagtgggga ggtggtccct ccagcggacc agggaagggg tcactgtgct 1680

```



203

gggagcagcc tccttgggcc tcaggaaacc accaagtgcc tcggatggtg gctgcccacg 1740  
gcgcttctgc tgagaccctg cccccggccc aggtgtctcg gaggtgggt ncccacggcc 1800  
tgggtgtggc tggaatggtg gcaggagtgg gcaccagtgc ggccccggtg gccatgggga 1860  
ataaaccagc attgctgcc aaaaaaaaaa aaaaaaaaaa aaaaaa 1905

&lt;210&gt; 263

&lt;211&gt; 1424

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 263

acccacgcgt ccgaaatttc aattctctgt gtaataccag agtagaagga gagggtgact 60  
ttaccgaact gacagccatt ggggaggcag atgcgggtgt ggaggtgtgg gctgaaggta 120  
gtgactgttt gattttaaaa agtgtgactg tcagtgtgat ctgttgcttt tctcaatgat 180  
tcagggatac aaatgggctt ctctcattca ttaaaagaaa acgcgacatc tttctaagat 240  
tctctgtggg aaaatgactg tcaataaaat gcgggtttct gggccattcg tcttactttc 300  
atthtttgat tacaaatttc tcttgacgca cacaattatg tctgctaate ctcttcttcc 360  
tagagagaga aactgtgctc cttcagtgtt gctgccataa aggggtttgg ggaatcgatt 420  
gtaaaagtcc cagggttctaa attaactaaa tgtgtacaga aatgaacgtg taagtaatgt 480  
ttctacaggt ctttgcaaca aactgtcact ttcgtctcca gcagaggag ctgtagggaat 540  
agtgtctcca gatgtgttct cccgtgtggg gccagcaat gggggcccct gatgccaaga 600  
gctctggagg ttcttgaaag aggggacacg aaggaggagt gactgggaag cctcccatgc 660  
caaggagggt ggaggtgccc tggaaatagc tgcctcatgc cacttaggcc atgactggat 720  
ttaatgtcag tgggtgtgcca cagtgcagag gctagacaac tgaaaggggc taccaaggct 780  
gggaaaaaaa tgcaattgtt gctgtgagtg actttgaaag actctggtgc cttgtggtgc 840  
ccttctgaaa ttcaaacagt aatgcaaaag tgtctgcatt agaatttacg gtgtctaaaa 900  
ttcatgtttt taaaagagct tgcctacaga tggtttccac acttgaaatt gtgccctgcg 960  
agttgcatag ctggaagttc aatgctcagt cctaccttgg ctcccattaa acatttggtg 1020  
ctctgtggat tgagttgaac gtgttgaggc tttgcaattt cacttggtgt aaaggctctg 1080  
gcatttttcc atttctatgc aaatttcttt gaagcagaat tgcttgcata tttcttctct 1140  
gccgtcacag aaagcagagt ttctttcaaa cttcactgag gcatcagttg ctctttggca 1200  
atgtccctta accatgatta ttaactaagt ttgtggcttg agtttacaaa ttctacttgt 1260  
tgcatgtatg ttcccatgta gtaagtcatt tttagtttgg ttgtgaaaaa accctgggct 1320  
gaagttggca tttcagttta aagaaaaaaa gaaactagtc ccagatttga aaacttgtaa 1380  
taaaattgaa actcactgga aaaaaaaaaa aaaaaaaaaa aaag 1424

&lt;210&gt; 264

&lt;211&gt; 1287

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (111)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (889)

&lt;223&gt; n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1196)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1229)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1284)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1287)  
<223> n equals a,t,g, or c

<400> 264  
tccgcgcccgc ctccgcccgc gaggaagaca ggcgcgcccgc cgcaccgccca gcgacccccgc 60  
ccgcagagtc ccaccgccac aggcctcggg ccagcggcca ggagctgcct nccccagccc 120  
ccgtcccgcg gccccagcc gcccccaacc ctgccccacg ggccccggcg catgagttag 180  
ctggagcaac tgagacagga ggccgagcag ctccggaacc agatccggga tgccccaaaa 240  
gcatgtgggg actcaacact gaccagatc acagctgggc tggacccagt ggggagaatc 300  
cagatgagga cccggaggac cctccgtggg cacctggcaa agatctatgc catgcactgg 360  
gggaccgact caaggtgct ggtcagcgcc tcccaggatg ggaagctcat catctgggac 420  
agctacacca ccaacaaggt ccacgccatc ccgctgcgct cctcctgggt aatgacctgt 480  
gcctacgcgc cctcaggga ctttgtggcc tgtggggggt tggacaacat ctgctccatc 540  
tacagcctca agaccgcga ggcaacgtca gggtcagccg ggagctgcct ggccacactg 600  
ggtacctgtc gtgttgccgc ttcctggatg acaaccaa catcaccagc tctggggata 660  
ccacctgtgc cctgtgggac attgagacag gccagcagac agtggggttt gctggacaca 720  
gtggggatgt gatgtccctg tccctggccc ccgatggccg cacgtttgtg tcaggcgcct 780  
gtgatgcctc tatcaagctg tgggacgtgc gggattccat gtgccgacag accttcacg 840  
gccatgaatc cgacatcaat gcagtggctt tcttcccaa cggctacgnc tttcaccacc 900  
ggctytgacg acgccamgtg ccgcctcttc gacctgcggg ccgatcagga gctcctcatg 960  
tactcccatg acaacatcat ctgtggcatc amctctgttg ccttctcgcg caggawcggc 1020  
tgctgctcgc tggctacgam gacttcaact gcaacatctg ggatgccatg aagggcgacc 1080  
gtgcaggagt cctcgttggc caccgacaacc gcgtgagtgc ctggggtca ccgacgatgg 1140  
catggctgtg gccacgggct cctgggactc cttcctcaag atctggaact aatggnccca 1200  
acccactg gccaagcca ggaaggggnc ctgccttccc cggggccaag gggccttggg 1260  
tccctgccct tccaaccaag ttngtn 1287

<210> 265  
<211> 991  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature

&lt;222&gt; (421)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (966)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 265

```
gtgggcatcc agctgttgaa taagacctgg aaggagatgc gggctacaca ggaggacttc 60
gacaaggtca tgcaggtggt gcgggagagc tggcccgcac tctggccctg aagcccactt 120
ccctggagct cttccgaacc aaggtgaatg cgctcactta tggggagggtg ctgcggctgc 180
ggcagactga acggctgcac caggagggca cactggctcc ccctatactg gagctgcggg 240
agaagctgaa gccagagctc atgggcctga tccgccagca gcgcttgctc cgctctgtg 300
aggggacgct cttccgcaag atcagcagcc ggcggcgcca ggataagctg tggttctgct 360
gcctgtcccc caaccacaag ctgctgcagt acggagacat ggaggagggc gccagcgct 420
naccctggag agtctgcccc agcaactccc tgtggccgac atgagggcac tcctgacagg 480
caaggactgc ccccatgtcc gggagaaggg ctccgggaag cagaacaagg acctctatga 540
gttggccttc tcaatcagct atgaccgtgg ggaggaggaa gcgtacctca acttcattgc 600
ccccccaag cgggagttct acctgtggac agatgggctc agtgccttgc tgggcagtcc 660
catgggcagc gagcagacac ggctggacct ggagcagctg ctgacctagg agaccaagct 720
gcgtctgctg gagctggaga acgtgcccac ccccgagcgg ccacccccctg tgccccacc 780
ccccaccaac ttcaacttct gctatgactg cagcatcgct gaaccttgac agtgtggctg 840
ccatgggcca cagctgcggc cactgcagca gccatgaagg gcagtgggta gaggagtgc 900
ggcaccctga ccagcagaga ttgctgcaga aataaagtct gcttggctct tgggawaaaa 960
aaaaanaaaa aaaaaaaaaa aaaaaaaaaa a 991
```

&lt;210&gt; 266

&lt;211&gt; 2320

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 266

```
tctccctccc tctccttccc gtgtgtccct ccccgcccg ctggaggctg ctccggaccg 60
ggacgcagag tctgcggacc cggcgccgag gcggccaccc gagacgcggc gcgcacgctc 120
cggcctgctc cgggcccggc catggcgggc ccccgcccg ctcccgcgat ctccgtttcg 180
gtctcgctc cggcttttta cgccccgcag aagaagtctg gccctgtggt ggcccaaaag 240
cccaaagtga atcccttccg gcccggggac agcgagcctc ccccgccacc cggggcccag 300
cgcgcacaga tgggcccgggt gggcgagatt ccccgccgc ccccggaaga ctttcccctg 360
cctccacctc cccttgcctg ggatggcgac gatgcagagg gtgctctggg aggtgccttc 420
ccgcgcctcc ctccccgat cgaggaatca tttccccctg cgctctgga ggaggagatc 480
ttcccttccc cgccgcctcc tccggaggag gagggagggc ctgaggcccc ataccgcccc 540
caccacagcc cagggagaag gtgagcagta ttgatttga gatcgactct ctgtcctcac 600
tgctggatga catgaccaag aatgatcctt tcaaaagccc ggtgtcatct ggatatgtgc 660
ccccaccagt ggccactcca ttcagttcca agtccagtac caagcctgca gccgggggca 720
cagcaccctt gcctccttgg aagtccccct ccagctccca gcctctgccc caggttccgg 780
ctccggctca gagccagaca cagttccatg ttcagcccca gccccagccc aagcctcagg 840
tccaactcca tgtccagtcc cagaccacgc ctgtgtcttt ggctaacacc cagccccgag 900
ggccccagc ctcactctcc gctccagccc ctaagtttcc tccagtgaact cctaagttta 960
ctcctgtggc ttccaagttc agtccctggag ccccggtgg atctgggtca caaccaaate 1020
aaaaattggg gcaccccgaa gctctttctg ctggcacagg ctcccctcaa cctccagct 1080
```

```

tcacctatgc ccagcagagg gagaagcccc gagtgcagga gaagcagcac cccgtgcccc 1140
caccggctca gaacccaaaac caggtgcgct cccctggggc cccagggccc ctgactctga 1200
aggaggtgga ggagctggag cagctgaccc agcagctaata gcaggacatg gagcatcctc 1260
agaggcagaa tgtggctgtc aacgaactct gcggccgatg ccatcaaccc ctggcccggg 1320
cgcagcagcc gtccgcgctc tagggcagct gttccacatc gcctgcttca cctgccacca 1380
gtgtgcgcag cagctccagg gccagcagtt ctacagtctg gagggggccc cgtactgcga 1440
gggctgttac actgacaccc tggagaagtg taacacctgc ggggagccca tctactgaccg 1500
catgctgagg gccacgggca aggcctatca cccgcaactgc ttcacctgtg tggctgtgcg 1560
ccgccccctg gaggggcacct ccttcatcgt ggaccaggcc aaccggcccc actgtgtccc 1620
cgactaccac aagcagtagc ccccgagggtg ctccgtctgc tctgagccca tcatgcctga 1680
gcctggccga gatgagactg tgcgagtggg cgcctgggac aagaacttcc acatgaagtg 1740
ttacaagtgt gaggactgag ggaagcccct gtcgattgag gcagatgaca atggctgctt 1800
ccccctggac ggtcacgtgc tctgtcggaa gtgccacact gctagagccc agacctgagt 1860
gaggacaggg cctcttcaga ccgcagtcca tgccccattg tggaccaccc acactgagac 1920
cacctgcccc caccctcagtt attgttttga tgtctagccc ctcccatttc caaccctccc 1980
ctagcatccc aggtgccctg acccaggacc caacatggtc tagggatgca ggatccccgc 2040
cctggggtct ggtcctcgcc catcctgcag ggattgccc cctgtctcca gacacccac 2100
ctgagggggg caccagggtt agtgctgctg ctttcaactg tgcacccgcg ccctcgccg 2160
gccccccgag cagcctttgt actctgcttg cggagggtg ggagaccctc caggacattc 2220
ccaccctccc ccatgctgcc aagttgtagc tatagctaca aataaaaaaa aaccttgttt 2280
tccagaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2320

```

<210> 267

<211> 423

<212> DNA

<213> Homo sapiens

<400> 267

```

aattcggcac gaggattgcc ctacccaag tcagtgtgtg gtggcccgaa ccttaggcaa 60
acagcaaaact gtcatggcca ttgctacaaa gattgcccta cagatgaact gcaagatggg 120
aggrgagctc tggaggggtg acatccccct gaagctcgtg atgatcgttg gcatcgattg 180
tkaccatgac atgacagctg ggcggaggtc aatcgagga tttgttgcca gcatcaatga 240
agggatgacc cgctggttct cagctgcat atttcaggat agaggacagg agctggtaga 300
tgggctcaaa gtctgcctgc aagcggtctt gagggcttgg aatagctgca atgagtacat 360
gccagccgg atcatcgtgt accgsgtggc gtaggagacg gccagytgaa aacactgggt 420
act 423

```

<210> 268

<211> 1846

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1776)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1816)

<223> n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1832)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 268

```
cgatttatca ggtttataat gcacttcagg agaaagttca ggcagtgtgt gcagatgttg 60
aaaagagtga gcgagttgtt gaatcttgtc aggcagaagt gaacaaatta agaagacaaa 120
tcactcagag gaaaaatgaa aaggaacaag aaagaagatt gcagcaggca gtgttaagca 180
gacagatgcc gtctgaaagc ttggacccag cgttcagtcc tcggatgccg tcctctgggt 240
ttgcagctga akgcagaagt aacttggag atgcagaggc ctcgatcct cctccccctt 300
actctgattt tcacccaaac aatcaagaaa gtactttgag ccactctcgc atggaaagga 360
gtgtctttat gcctcgacct caagctgtgg gctcttccaa ttatgcttcc accagtgccg 420
gactgaagta tcctggaagt ggggctgacc ttctctctcc ccaaagagca gctggagaca 480
gtggtgagga ttcagacgac agtgattatg aaaatttgat tgaccctaca gaggccttcta 540
atagtgaata ctcacattca aaggattctc gacccatggc acatcccgac gaggacccca 600
ggaacactca gacctccag atttaactaa acaaagaaa ctctccacct agcactgttt 660
ttcttcattg cttactgaga gggtttttga gaacttaatc tggggggaga actgctttct 720
cagatacctt aactcccgag aagagagtcc ttgtgcacag aacttggtgg agcctccatc 780
cgctgctctt taccttttga tacagtgtgc aagtttcatg acagaatcat taagataatc 840
aaattgtcct aattctgtgt cgattcatgg atatactggt aaatttaggc aaagtgaaac 900
ttatcagcgt agtttctgtt ctttaaaata aattggaaat tagagactaa gcacaattag 960
tctataaatg ttctataaat caaaaactta cctcttgac tatcatgcct tgaaatttac 1020
tttttcaaag ggaaacaagt ttagcagcag ctttcaaaga acttctttct atgatgagcc 1080
aaattcatct ttgccagaaa agaaattttg ataattccaa gaagcctgat tagaacaat 1140
cagatatacc ttctcttgtc tgcagtactt tgtgagataa aagagagggc ttccaacttt 1200
tttctactag cttgatatgt attatcactt aaaatggttg cttttaaaaa aaaaaagtag 1260
rgatactaata taccagtaag taatcatcca aataaatacg tcataaaaata aattaattat 1320
tttttcyttg atggattaca gtgactactg tgttgcactg gcacatttat ggtctctgtt 1380
ctggaatctt ggaggacaca cagcagtgga gaacagaagg agtgagtttt ataatgaaca 1440
gattccagac acggtagggt tagctgagtt catacagagg agatataact catttagatc 1500
ttctgacaaa tcctagtgtt agttttatct gtggaggaaa gacatttaat aataaactgt 1560
ttgggaatct tgggtaataa agattcattt tcaagctgaa taaccatact tattttattt 1620
taagttgcca tttggggaat aagtgcattc caagagagtc tctacacatc ctggaagtcg 1680
tcaatgattt ccctttggaa actactttat ttactaatt taaactatct tgtactgatg 1740
tagccctgag gtagttcatg aaaatgctgt gcactncatt ccatgggaat gaaatgttgg 1800
aaagctgatac ttttcnggat ataaaatggt gnatgatgaa aaaaaa 1846
```

&lt;210&gt; 269

&lt;211&gt; 601

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (536)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (556)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 269

```
ggcacgagct ggggaggagg ggggtggtgac acggtggaga caccggctag gccagggggc 60
ctgcccttgg gacaggtcca gacccatgga gcccccggg aggagcagca ggtccacagc 120
gtctcatact ctacaccagt attgctgtcc tactcaggtc cttgactcca tgaagcttac 180
cccctcaggc aggctggcag agagcaggga agaggaggag gaggaggaga ctgagggaaga 240
ggaagaggaa gacgctcacc agttctgctg tccggcctcc gagtgcagta gtccctcctc 300
tcggttaactg agaggacaag ggccattttc tatgcagaag caaaagcctt aaccagsccc 360
tccttcccc caccacccc cccgcagatt cccccatggg accctgtccc ctgcttcagg 420
aaccagatgg gcaagcatcg tgccccttcc tccccccacc ttcttcttgg aattcccatc 480
cccactgctg tctcctctgg actccagccc ctgaattaaa gaaactggag ccctangtcc 540
gactaaaatt tggganaagc aaacttgagc ttggacttgg aactggatcc tcccgtaccc 600
g 601
```

&lt;210&gt; 270

&lt;211&gt; 880

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (876)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 270

```
aattcggcag agggaaaggg tgggggtcag cctccccaaa atcacatgga ttccccaaagt 60
ggaaactagg agcagggagt tgcttgggtg gccgctaaca ccaggctact cttatttttag 120
cttgctaagt tgagatcagc tagacctgct ttcttttctc ctcagtcttg catttccctc 180
aatacaagct gcagcctctt tcctcgtttc tagtctcaga aggaaggaga gggaaagccat 240
tctcctctag ggactcttca gtctcattta gatgatagtc ctttttttcc tacctccata 300
ttagagatgg agctccttcc ttttcctggt tcttaatttt tgtcttctca ttctgcttcc 360
cctctcaccc tattgccagt tccaccaact agagtgaag acttcctagc catttcatta 420
aatctattct gtatccacca ggtggcagca tcttgtcata cgtgtcagga cttaggactg 480
cggggttttag gttagatgtc acggaaaaag ctagttctgt ggtcaggcgg caccaatgag 540
aaaggaatgc agaccctcca gatgtatcct tgggaaaagc agtaaaccac ctaatattta 600
ttgaagacct actttgtcct ctacataggg tagcttctgt cagggaatct tggttcttcc 660
caagaaacac tgattttctt tcaggagagc ttcatgtgtt catttatctc caccacagca 720
gattttaaga aattataata tgtaaatatt gatatttata aagagtatat ctaacgtgaa 780
taaattatga agcatactaa tgagtaccta tgaccataaa cacatatata ttaaaacatt 840
ttaaatacca aaaaaaaaaa aaaaaaaaaa aaaaanaaaa 880
```

&lt;210&gt; 271

&lt;211&gt; 2484

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (194)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (623)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2396)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2484)

<223> n equals a,t,g, or c

<400> 271

```

aaggagatga ggggccgtga aggggaaccc aggaaactga gtcctgaaag caaggaggaa 60
cttccagaat gaaggcgccc gacactcctt cctgcctttg ctcaagcggg tccttcaccc 120
cgatcaagtt ccttcccatt tctccatctg ggggacctg aacgtgcaca tcctcagaga 180
agccctcctg gggntctcca attctagttt attgccccct cctatcgatc cccagcgcg 240
ctcatcgggc ctgtggacaa ggacaggttt gaagagagga ttccctggat cgcggaaggg 300
ctgcaggaat ggcacagccc cttccgagga tgccaaagga gcccgggcaa aggaaagtgg 360
ccgtgcccgg cctgcctacc actagatccc caccaccta tgactgctca gtcccgtct 420
cctaccacac ccacctttcc cggcccaagc cagcgcaccc cgctgactcc ctgcccagtc 480
caaactccaa ggctgggcaa ggcactgatc cactgctgga cagacccggg gcagcctctg 540
ggtgaacagc agcgtgtccg ccggcagcga accgagacca gcgagccgac catgcggtg 600
cacagacttc gtgcgcggct gancgcggtg ggcctgtggg yttctgctgc ttcttgctcg 660
gggccagggc caggactcag ccagtcccat ccggaccaca cacacggggc aggtgctggg 720
gagtcttgtc catgtgaagg gcgccaatgc cggggtccaa accttccttg gaattccatt 780
tgccaagcca cctctaggtc cgctgcgatt tgcacccctt gagccccctg aatcttgagg 840
tggtgtgagg gatggaacca cccatccggc catgtgtcta caggacctca ccgcagtggg 900
gtcagagttt cttagccagt tcaacatgac cttcccttcc gactccatgt ctgaggactg 960
cctgtacctc agcatctaca cgccggccca tagccatgaa ggctctaacc tgccggtgat 1020
ggtgtggatc cacggtggtg cgcttggttt tggcatggct tccttgatg atggttccat 1080
gctggctgcc ttggagaacg tgggtggtgt catcatccag taccgctgg gtgtcctggg 1140
cttcttcagc actggagaca agcacgcaac cggcaactgg ggctacctg accaagtggc 1200
tgactacgc tgggtccagc agaatatcgc ccactttgga ggcaaccctg accgtgtcac 1260
catttttggc gagtctgcgg gtggcacgag tgtgtcttcg cttgttgtgt ccccatatc 1320
ccaaggactc ttccacggag ccatcatgga gagtggcgtg gccctcctgc ccggcctcat 1380
tgccagctca gctgatgtca tctccacggt ggtggccaac ctgtctgcct gtgaccaagt 1440
tgactctgag gccctggtgg gctgcctgcg gggcaagagt aaagaggaga ttcttgcaat 1500
taacaagcct ttcaagatga tccccggagt ggtggatggg gtcttcctgc ccaggcacc 1560
ccaggagctg ctggcctctg ccgactttca gcctgtccct agcattgttg gtgtcaacaa 1620
caatgaattc ggctggctca tccccagggt catgaggatc tatgataccc agaaggaaat 1680
ggacagagag gcctcccagg ctgctctgca gaaaatgtta acgctgctga tgttgccctc 1740
tacatttggt gacctgctga gggaggagta cattggggac aatggggatc ccagaccct 1800
ccaagcgag ttccaggaga tgatggcgga ctccatgttt gtgatccctg cactccaagt 1860
agcacatttt cagtgttccc gggccctgt gtacttctac gaggttccag atcagcccag 1920
ctggctcaag aacatcaggc caccgcacat gaaggcagac catggtgatg agcttccttt 1980

```

210

```

tgttttcaga agtttctttg ggggcaacta cattaaattc actgaggaag aggagcagct 2040
aagcaggaag atgatgaagt actgggccaa ctttgcgaga aatgggaacc ccaatggcga 2100
gggtctgcc aactggccgc tgttcgacca ggaggagcaa tacctgcagc tgaacctaca 2160
gcctgcggtg ggcggggctc tgaaggccca caggctccag ttctggaaga aggcgctgcc 2220
ccaaaagatc caggagctcg aggagcctga agagagacac acagagctgt agctccctgt 2280
gccggggagg aggggggtggg ttcgctgaca ggcgagggtc agcctgctgt gcccacacac 2340
accactaag gagaaagaag ttgattcctt cattcamttt sgscattcat tcatanttcc 2400
gtccatccat tcagaaagcw tttatttaag attttayttc agggmtwgat kggcccatat 2460
tgtaatttc cccgtttttt gggn 2484

```

&lt;210&gt; 272

&lt;211&gt; 751

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 272

```

agccaccgcg tgaccactg cccctatgcc gtggccctac ccgaggtggc cccagcccag 60
ccactcaccg aggcactgag ggctctctgc cacgtggggc tctttractt cgccttttgt 120
gccttgtttg actgcraccg ccctgtgsg cagaagtctt gtgacctcct tctcttcctg 180
agggacaaga ttgcttccta cagcagcctg cgggaggcca ggggcagccc caactactg 240
tccgcagagg ccamcctgcc gaggtggcgg gcgggtgagc aggccagccc cccaggggac 300
caggagcctg aggtgtgtct ggccatgctc aggtccctag acctggaggg cctgcggagc 360
acgtgtggcg agagcagcga ccacgtggaa aagagtcccc agtccctcct gcaggacatg 420
ctggccacgg gaggttctc gcagggggac gagggcgact gctactgagc agaaccagag 480
tctgccactg gggctcagga ccaagggagg cagcaccatg tccttctgtg ggacactgcc 540
agccccaggc tccagcccag cccggtggat cctctgggga agccaggacc aggagagaag 600
caaggtcaag aaatcccaca gtttgatgta ttaaagaaat gacttatctt tactcaaaat 660
aaatggcatt gaagtcttct ttttaacctt tatgagttaa ttttaataata atgatctgag 720
acaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 751

```

&lt;210&gt; 273

&lt;211&gt; 3309

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (3279)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 273

```

agaagcagga gggagaaggg cagacagggg tcggttgagc cagggtagaa accaagggga 60
gccagggtag aaaccaaggg gtcagggtcg ggctggagga cacgggtgag gtcctcccaa 120
aactgggccc atgtggtgtg acatccccac cagcctcaga tgagacgggc caggacgccc 180
agccacagca agcctgttcc ctttgccgga tccccaaaca ctagagaagc tctcctaacc 240
caaggcggag aatgaagggt gtggcggcag aggaggaggg cagcagctga gaggccaggg 300
acagggtgcc tcgccaagct gtctgaggtc tgtcccaggt gggccagggt gtgcaggtag 360
aacagggtga ggagaggggg tcggctcarc aggaggaggc tgtggctgca gagcctggg 420
gagcttttag gtgttgagat ggggcagctc tgaatcctag accctggaat agcctgtccc 480
ttttctctgg gtctcgtggg ggagccatga tctgggctgc tctcttgggg acactgggtg 540
gtggttacac agttgacctc tgctggctc ccccttggtg caactcctgc ctccatcccc 600

```



cttgctgggg tccccctc atc cacttgaggg cgcctgaggg ccaggarcag caggcaagga 660  
gcctgggtct aggctaaggg ggktktgcy cacctcctcc ctgaccctta acactcctgt 720  
cctgcccaga ccaacagaga gagctgtccc tgagaccccg gagagaagca gctgccgaaa 780  
gctgcagcct ttccgcactc tgagaccatg atcttcctcc tgccagggga gagccacca 840  
caggccatgt ccagcccac ttccctcagc cccaggggt tcttctggt ccctctgagg 900  
attccctagg gctgccccgc agagggggtt cccaagctc tgttttgaag cctgcaatgt 960  
ggaaaagtga gaagtcagag ggaacaggac aggtgcagcc gggctctgag gccacacctc 1020  
acacctcgct gttccccaac atccctgag cagtgtgagc tcatctcacc agatgagaag 1080  
aggccctgtg catttytttt gtttgtttgt tgctgttttc cccacccat ccagtctctc 1140  
tcagcaaagc aaattcctta acacctttgg tggagaattt cttaccaga cttggggctg 1200  
tgatgccctt cagtgcgtgg tgagtgcagc gtgtgtgctg gtgctgtgt gtgaacctgg 1260  
gggcatcctt ggtggcctgg gagcgtgagg agaggcccc tgtgtgctgg gtgagtgggt 1320  
ggtgtgggg caatgcagtg aggtctctct ggtgaggctc ccaacctggc agtccccagc 1380  
ctccagcat ctgtgagcgt ctgttgact ttacagaaga gcctcatccy gtctgcccct 1440  
cactctgccc tggaatcaac atctccgag tcttctgtg gggaaatagc agagcccac 1500  
ttaactccat aaactgcttc ccattccgca gccagttct gattgttgag gtgtcgctc 1560  
gttccaggtc cccagtcctc ctcttctctc tgctctctc ctgtcctca cctccccact 1620  
ccagccccgg ctcagttcag ggaaatgctg ttccayatca gccctctgct ctctgaggca 1680  
gccgcgctc tgactcgag ctactgaaa cttctgctc tgctaggatt ggagtctacc 1740  
tatctcttcc atttgcctca gctggagttc tggaaacttc ctctcgagg tgggggtggg 1800  
ggttgttaag gatgtgggg ggcctgggga aggaaggagt tcagaggaa ggtgtcccc 1860  
gtctcttga tgtaccctc cgctcctggg acacgtgctc tctctgtctc tgggtcttct 1920  
ggctgtgcac gtttgtgtgt ccttgtaaat atgttttagg aagaaagcaa aagggactga 1980  
actagcctct ggtaggattg caggggtcca gccttgctg tttccgaagc cccacactg 2040  
cctttcgccc cactgagact ggtccctca aaaggtagac aaaacagcag ctccctgtgg 2100  
agctgaaggg cggcctcaaa gtggcttttt gttagacaag gtttaagggtt cctcatgagc 2160  
aagggtgcag atcggtcctt cctcagctcc ttgatttgtg acctgacca aggggcctgc 2220  
caccagccc ctccagtgc ctctcctcga tgctcgctc ctctcctgccc cactccccct 2280  
ggcttaggca ggtaggggaa tttagggcat gctggaagaa gcttaaccat gtgtcaaaag 2340  
aacggtttct tgcttgcttg gtcttggaac tcccttggtc tgccccaggg ctcttggtgg 2400  
catgggtgct gggggaggtg gatgtcagat ctggtaggt gcagcagaga aaataaatgt 2460  
gccttgagag accactcaga gaggttccaa ggggtgatga gaaggaaagca tggcctggga 2520  
gcttggaagg raggggtggt ggggtggcggc atcttgactg cccctgttg tcccacactg 2580  
gggggtggt caccctctc actccagccc gcctgcctc agccttccat gagcttcacc 2640  
tgcttccaac ttacttttg aggggtggg gtccgttggt atcaacacgg ggacctctg 2700  
cttcacaaa gcccgagccc tcagccctg gggagaacaa atggctgagc ttgataacct 2760  
ggggtcgctg agaggctgc ggtggcggc agtcccagg gagagacacc acagaaggag 2820  
accagacat cccgaggaa ttcccagcag agcaaaactg tttccagcct gaagcctgct 2880  
taaaactgtg gatgtgcaat aactgagctt agagttagga attgtgttca agtgcttga 2940  
tttccgtctg tagatttaac tgctgaaatt gtatctctca gtaatttttag atgtctttta 3000  
aaaaattgaa aaacaaagt ttagactgtg tgcgtgtgcg ttgatgggca ctcaagagtc 3060  
ccgtgagtca tccagccctg cctttccct gcgccccat cctctcacgt cccgcccyc 3120  
ctccacttg ggacctgct tcgtgtgctc ttatctgctc tattactcag cctaaggaaa 3180  
caagtacact ccacacatgc ataaaggaaa tcaaatgtta tttttaagaa aatggaaaat 3240  
aaaaacttta taaacaccaa aaaaaaaaaa aaaaaccng gggggggggc ggtaaccat 3300  
ttcgctaa 3309

&lt;210&gt; 274

&lt;211&gt; 843

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (780)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (833)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 274

```
cgcgagcggg tgagaggccg cggcggcagg tccacctggg cttgcgaagg cacagattcc 60
ccgtcccacag ctcacgacca gatgcaccag caggagtcca catcgaggac gtccctccggg 120
cactcccacg accagtgacc aggagttaaa ctttgggatg tgcccgtgat gttggaccac 180
aaggacttag aggccgaaat ccaccccttg aaaaatgaag aaagaaaatc gcaggaaaat 240
ctgggaaatc catcaaaaaa tgaggataay gtgaaaagcg cgcctccaca gtcccggctc 300
tcccgggtgcc gagcggcggc gttttttctt tcattgtttc tctgcctttt tgtggtgttc 360
gtcgtctcat tcgtcatccc gtgtccagac cggccggcgt cacagcgaat gtggaggata 420
gactacagtg ccgctgttat ctatgacttt ctggctgtgg atgatataaa cggggacagg 480
atccaagatg ttctttttct ttataaaaac accaacagca gcaacaattt cagccgatcc 540
tgtgtggacg aaggcttttc ctctccctgc acctttgcag ctgctgtgtc gggggccaac 600
gcagcacgct ctgggagwga cctgtggccc aagacgtggc cctcgtggag tgtgtgtgtc 660
cccagccaag aggcagttag gcaccttctg cctgcatcct ggtgggcaga cccagttcct 720
tcattgcagt caactgtgtc acaggggaaa ccttggaac cacagccagc agttcagggn 780
gaatggtcca tctgagcctt ttgtgcagtt gctgatgtgg agttcgatgg ggncccaaac 840
tgt 843
```

&lt;210&gt; 275

&lt;211&gt; 2028

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 275

```
tcggcacgag gtttttgatt tatggataat ttcttaagag tacacacttt agatacacia 60
ataatcgttc atttaccatc tttaggatca ttgaaactca tctcactaaa gaaagttcac 120
ttgaacctct ttatagcatt gatactaggt gaacagaaat tacctgacta ataatttgtc 180
taacatcata tatcagaatt ttattgtata tgatgaacaa aacttaaaat tttttaaaat 240
taattyttaa atactgtttc agagtcttaa aaaggcagtt ttttaaaaaa cttaagttga 300
taaaaactgt aagaataatt tagcagaaat agaaccagaa tgtagaagag tagtcatgta 360
acagcagtaa taacatactt cagcttccat ataggaatag aagtggtaga gccaaaagtg 420
atthaggaag agttataagg tacagggtga gtatcccttt tccaaaaatg cttgggacaa 480
gaagtatttc agatttcata atttttttca aagtttgga tatttgcat atacttacca 540
gttgggcac ccaaatctga aatctgaaat gttccatgag catttccttt gagtgcacg 600
ttggcactca aaaagggtca acattgagtc cacttaacac ttaggtgtta gaagacctaa 660
ctttctgtaa caattaacct tatactttgt ttgtcatcga atatttgtt aatgcacgtc 720
aggtaatggt ctgtattgtg atagcttcaa ggtggaacat actgtaactc ccagatgcta 780
ggaagttagt ctaataattc actgcagaaa atgattaaag tggctgtcct tttaattaa 840
agtgtggagt cataaactta agttctcat atagtacaa gagtccctag agattgttat 900
tcaagttcct tagaaattgt tatttaggta taatcatc tttgtcttga ctagagcttg 960
aaaccttggt atctgattgt gtaccactcc aaattccctg cttctgcaa gttgaatgtc 1020
```

```

ttgctgaatg tgtctagggg ttcattctca gtaatcgaca ttccactagt gccatagtta 1080
acttcatgac atgtagacat tcaaaacttg agccttggat gttcctgtgg acctgacagt 1140
taaaaaatata aagaacctag gattcaattc caactttctc tgtttgctt gggttgaata 1200
acttatcttk tggagaatag ctttaagtgg cttagacact gataaaattc agctgtgttg 1260
ttgacgctca tctcttttgt cttacgctta gccatattta aatcttgaat ttaatagagt 1320
ctagtgaata aaatgagtgg gaagaatgaa tataaaagta ataataaag gaaaaagga 1380
aagtaaaacta tttagaatgt agttttgtta tattcccagc atttcaatat ttattagtta 1440
cttgtaaaatt actgtggctg tgtagtttat aaatgtctgt gcactatatt aattagaaga 1500
ccatagaaca tgccagcagg ttggctaata ctatgggggt ttttaccaca gttgccattg 1560
tggaagaaat tatttggtac attaataaaa aaagtggta aaacatgrtt ttatacctca 1620
gtgtataaga tgtgcaagac aaatatgctt atttcctttt ctagaatata agtgatatta 1680
tttgcttatg aactaacac tattaatgac aggagtcaat cagcctttac agctatcaaa 1740
atataatgag atcccaatga tgattctttt ttactttgaa tgttaattag ttgggactt 1800
tgattggctg gcaaacattt tatcattgtc agaatttaat ttagatttca aaaatagctt 1860
acaggatttt aaacatgggt tgggtattct aagccttttt tttaaaaaaa gagatctttt 1920
tgagagaaac aaatgaggat tgtaaagttt ggggacttac ctctgtagca ttgtgaaaat 1980
aaactttgat taagctgaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaa 2028

```

<210> 276

<211> 1455

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (759)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1408)

<223> n equals a,t,g, or c

<400> 276

```

tcgaccacg cgtccgcggc aatggcgggtg gcgctgcggg gattaggagg gcgcttccgg 60
tgccggacgc aggccgtggc gggcgggggtg cggggcgcg cgcggggcgc acagcaggtc 120
agcgggacta tgatctcctg gtggtcggcg ggggatctgg tggcctggct tgtgccaagg 180
aggccgctca gctgggaagg aaggtggccg tgggtggacta cgtggaacct tctccccaag 240
gcacccgggtg gggcctyggc ggcacctgcg tcaacgtggg ctgcatcccc aagaagctga 300
tgcaccaggc ggcactgctg ggaggcctga tccaagatgc ccccaactat ggctgggarg 360
tgccccarcc cgtgccgcat gactggagga agatggcaga agctgttcaa aatcacgtga 420
aatccttgaa ctggggccac cgtgtccagc ttcaggacar aaaagtyaag tactttaaca 480
tcaaagccag ctttgttgac gagcacacgg tttgcggcgt tgcaaagggt ggaaagagat 540
tctgctgtca gccgatcaca tcatcattgc tactggaggg cggccgagat accccacgca 600
catogaaggt gccttggaat atggaatcac aagtgatgac atcttctggc tgaaggaaatc 660
ccctggaaaa acgttgggtg tcggggccag ctatgtggcc tgggagtgtg ctggcttcct 720
caccgggatt gggctggaca ccaccatcat gatgcgcanc cscctccgc ggcttcgacc 780
agcaaatgtc ctccatggtc atagagcaca tggcatctca tggcaccggg ttccctgagg 840
gctgtgcccc ytcgcggtc aggaggtcc ctgatggcca gctgcaggtc acctgggagg 900
acagcaccac cggcaaggag gacacgggca ctttgacac cgtcctgtgg gccataggtc 960
gagtcaccga caccagaagt ctgaatttgg agaaggctgg ggtagatact agccccgaca 1020

```

```

ctcagaagat cctggtggac tcccgggaag ccacctctgt gccccacatc tacgccattg 1080
gtgacgtggt ggaggggagg cctgagctga caccacacagc gatcatggcc gggaggctcc 1140
tggtgcagcg gctcttcggc gggtcctcag atctgatgga ctacgacaat gttcccacga 1200
ccgtcttcac cccgctggag tatggctgtg tggggtgtc cgaggaggag gcagtggctc 1260
gccacgggca ggagcatgtt gaggtctatc acgcccatta taaaccactg gagttcacgg 1320
tggtgggacg agatgcatcc cagtgttatg taaagatggt gtgcctgagg gagccccac 1380
agctggtgct gggcctgcat ttcttggncc caacgcaggc aaattactca aggatttgct 1440
ctggggacaa gtgtg                                     1455

```

&lt;210&gt; 277

&lt;211&gt; 1923

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1814)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 277

```

ggccctgccc acccaggccg caagagctgc cgggacggtc cccatcttct tggagcgctt 60
taggctggcc ggcgggcgctg ggaggtggag tcgttgctgt tgctgtttgt gagcctgtgg 120
cgcggtcttct gtggggccga accttaaaga tagccgcaat ggctgaaaat ggtgataatg 180
aaaagatggc tgccctggag gccaaaatct gtcatcaaat tgagtattat tttggcgact 240
tcaatttgcc acgggacaaag tttctaaagg aacagataaa actggatgaa ggctgggtac 300
ctttggagat aatgataaaa ttcaacaggt tgaaccgtct aacaacagac tttaatgtaa 360
ttgtggaagc attgagcaaa tccaaggcag aactcatgga aatcagtga gataaaacta 420
aaatcagaag gtctccaagc aaacccttac ctgaagtgc tgatgagtat aaaaatgatg 480
taaaaaacag atctgtttat attaaaggct tcccaactga tgcaactctt gatgacataa 540
aagaatggtt agaagataaa ggtcaagtac taaatattca gatgagaaga acattgcata 600
aagcatttaa gggatcaatt tttgttgtgt ttgatagcat tgaatctgct aagaaatttg 660
tagagacccc tggccagaag tacaagaaa cagacctgct aatacttttc aaggacgatt 720
actttgccaa aaaaaatgaa gaaagaaaac aaaataaagt ggaagctaaa ttaagagcta 780
aacaggagca agaagcaaaa caaaagttag aagaagatgc tgaaatgaaa tctctagaag 840
aaaagattgg atgcttgctg aaattttcgg gtgattttaga tgatcagacc tgtagagaag 900
atttacacat acttttctca aatcatgggt aaataaaatg gatagacttc gtcagaggag 960
caaaagaggg gataattcta tttaaagaaa aagccaagga agcattgggt aaagccaaag 1020
atgcaataaa tggtaacctc caattaagga acaaagaagt gacttgggaa gtactagaag 1080
gagaggtgga aaaagaagca ctgaagaaaa taatagaaga ccaacaagaa tccctaaaca 1140
aatggaagtc aaaaggtcgt agatttaaag gaaaaggaaa gggtaataaa gctgcccagc 1200
ctgggtctgg taaaggaaaa gtacagtttc agggcaagaa aacgaaattt gctagtgatg 1260
atgaacatga tgaacatgat gaaaatggtg caactggacc tgtgaaaaga gcaagagaag 1320
aaacagacaa agaagaacct gcatccaaac aacagaaaac agaaaatggt gctggagacc 1380
agtagtttag taaaccaatt ttttattcat tttaaatagg ttttaaacga cttttgtttg 1440
cggggccttt aaaaggaaaa ccgaattagg tccacttcaa tgtccacctg tgagaaagga 1500
aaaatttttt tgtgttttaa cttgtctttt tgttatgcaa atgagatttc tttgaatgta 1560
ttgttctgtt tgtgttattt cagatgattc aaatatcaaa aggaagattc ttccattaaa 1620
ttgcctttgt aatatgagaa tgtattagta caaactaact aataaaaatat atactatatg 1680
aaaagagcaa aaacagtttt tgattttttt tttctttttg tacccaaagc atttaggaaa 1740
gaactagaat attgctattt gacgatgggc ctttcccaca ggccatttat ggtgtctcct 1800
aggctgggct ttgnatattt acacaggaaa gttgggtaac actagaaata attacttggt 1860

```

cacaaagcct tccctttttt tttccttttc gagactgagt ctactccta tcgcgcagct 1920  
gga 1923

<210> 278

<211> 1380

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1293)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1297)

<223> n equals a,t,g, or c

<400> 278

aggggaagaa ggggtgggct ccccttctgg gatccttgcc acccccctcc gcagcgcgcg 60  
cggaacgaca cacacacaca cacacacaca cactcgcata ctcatgcaca 120  
ttttccttca tttccagatc ctttatttca gagcagccca ttttcctctg gattcattga 180  
tgaatacaag tacccacacc tttggccagt aatgtcagtt acctgctgca ggttctgtgt 240  
atgaggcctt catgaacggg taccttctcc atacactagg gaagcatttg tcagactctg 300  
cagactgggt tctagagagg cagagtcttt aagagtattc atttcttctg gaagggtggag 360  
ctttacccaa agtggaagtt agccttgctc aaagatgtgt tttgtggtag gtggtaaaaa 420  
taaataaata aataaataat aaaaaaagaa acatgtattg gaggtaattt gacactgctg 480  
ctggcagtag ttctctattc accattttta agcccattca ggttctctct tcctgaaaag 540  
aactgattgc tgtgtttaca tgaaatgaca ttggagtcag atggtctggt ttaaagattt 600  
ccatgacagc ctcttttcct gagtgggaga gattggaggt ggtctatccg tacgatgtgg 660  
aatcaaacgg tgggtttctt agtagctaaa gaagccatgt acttctagtg tgtttctcag 720  
aatatcaact catgttcttc agatgctttt ctttttttaa tgggtaggga aaaggataaa 780  
tttgggattc cacagtgcct tgcatatagt aggcgcccag taaatacttg ttgaagcaaa 840  
ccaagtttcc caagtctcca tctcttatag tgaccaagac atctttctcc tctgaagggc 900  
ttggcagttg tggctaaaaa ataagcagta tcattatttg cttgaaatca tatatacagt 960  
ttgtatgaat ttcagtatgt tgccaagaca tgatttttct ttattgtatt ttctgtaaat 1020  
atctctggca ctgaactgta aagtaaaggc aaagtgtaaa tatgaaggcg tgcccgtagc 1080  
ccttgccctc tgtgtttcat cttcgctcgt tagggaagaa ggtccagagg tttgtttgta 1140  
tttatgccga tcctttgtcc agaagaagcc catggaatat tgaatgtaat acatttagtc 1200  
aattaaattt taaggagatt cttatctaata aacttttgtg gtgcttttgg atacaggctg 1260  
aggctttact cctacactgg tgctgttaat ttncacnttt caggggatgt ctgctcggct 1320  
ttggctgccc ttataaattt agatctgtag tttaaataaa cattaaatga gtatttcagt 1380

<210> 279

<211> 1018

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (818)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1017)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1018)

<223> n equals a,t,g, or c

<400> 279

```
catggccgcg cccgcccggg cctcatctcg gtgttctcga gttcccagga gctgggtgcg 60
gcgctagcgc agctggttgg cccagcgcgc asatgctgcc tggcaggggc ccgcgcccgt 120
ttcgcgctcg gcttgtcggg cgggagctcg tctcgatgct agcccgcgag ctaccgcgcg 180
ccgtcgcccc tgccgggcca gctagcttag cgcgctggac gctgggcttc tgcgacgagc 240
gcctcgtgcc cttcgatcac gccgagagca cgtacggcct ctaccggacg catcttctct 300
ccagactgcc gatcccagaa agccagggtga tcaccattaa ccccgagctg cctgtggagg 360
aggcggctga ggactacgcc aagaagctga gacaggcatt ccaaggggac tccatcccgg 420
ttttcgacct gctgatcctg ggggtgggcc ccgatggtca cacctgctca ctcttcccag 480
accaccccct cctacaggag cgggagaaga ttgtggctcc catcagtgc tccccgaagc 540
caccgccaca gcgtgtgacc ctcacrctac ctgtcctgaa tgcagcacga actgtcatct 600
ttgtggcaac tggagaaggc aaggcagctg ttctgaagcg cattttggag gaccaggagg 660
aaaacccgct gcccgccgcc ctggtccagc cccacaccgg gaaactgtgc tggttcttgg 720
acgaggcggc cgcccgcctc ctgaccgtgc ccttcgagaa gcattccact ttgtagctgg 780
ccagaggggac gccgcagctg ggaccaggca cgcggccnat ggggctgggc ccctgctggc 840
cgccactctc cgggctctcc ttcaaaaag ccacgtcgtg ctgctgctgg aagccaacag 900
ctccggccag cagccctacc cggggctcaa cacacaggct gtggctctgg acatccggat 960
attaaaagga gcgttgctgg aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaann 1018
```

<210> 280

<211> 1192

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1105)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1130)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1154)

<223> n equals a,t,g, or c

&lt;400&gt; 280

```

tccgggaatt cccgggtcga cccacgcgtc cgctctgttt atatagcagg tgtcacaact 60
aacttgtctt tagccttgggt gctttgatcc ttctatatatt tgacccca ggtgtggtcc 120
ggtttactta atcaggacat gggcctaaga acaaaccttt tcccttcatg ataacatcca 180
tagacaactt attagaaggg actagagttt ttgcaaattt ccctgctgga tggggcctat 240
agctatactt agtatatgcc taaacatggt aattggatag taaatggttt tctagtcca 300
ttgctgtata ttgcctaaa tggacttgtg ttcaaattat ttcttcaatt gtcatagata 360
atcctgtacc aaatggggaa gaattaggaa ataatcatgt tgtctaattg tactctggat 420
tcagggcagc aactgccatt taaatgttgt cttgttcatt tctaaatctg ttccatgaag 480
tttaggtttt ccctgaaact aagtgaatt atttccaaaa tgaaacaggc ttctcaggga 540
catatccact tcttcccagt ctgcctttgg attaaagcac caagcagaga ccacattaat 600
tccctttgct atactgtgat ccttagtatg ttaattctta agaaaccaac atatcactga 660
aagaaggctg gcagaacgca agtgcathtt ttcactgtgg gaagaaagat caagtacgt 720
attathtttt cctggttgtc acttaattggg ctgagtaaaa agcttgaaaa ctcagacttt 780
cggctcttgt tctgccactc attggttatg aggaggccca gagcaggtaa gttcaccttc 840
ctggccttac tttcctgatg tgtaatacgg aattacttca cagtagcatg acagtataag 900
acaccagcag tagatacaac tatgatgaca ttccatgagt tgggtatttt agttctaact 960
gctaaatttg ttctctttac gggacagatt tctaataaag tgcttggtct taaaatacat 1020
ggttgacagc aggtgccta tcccttaact ttgaggcag gtgctacctt ttggggatat 1080
ttatttttaa atttttaata ctttnggtac tccaattgtc cagtgttccn tgggtgttgt 1140
athttttatt tttnggggat agtggggggg ccttaagggg gaggagggat ag 1192

```

&lt;210&gt; 281

&lt;211&gt; 1755

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 281

```

aaattacagg aacggagtaa gaacgtaaga aatcgcaaag cacgtgaacg tatgggaatc 60
tactgttctt tggcccttct cccgaccctg agccctgtct tgctacgact gcgtgggtga 120
agtcgtctat aaaaactcat ctctgcgcgt ctcttcgccca cattcgcttc ctgctttcgg 180
tgtgtctgtt gtgtcttgtt gcgggcaccg cagtcgccgt gaagatggcg tctaccagcc 240
gtttggatgc tcttccaaga gtcacatgtc caaaccatcc agatgcgatt ttagtgagg 300
actacagagc cggatgatgt atctgtcctg aatgtggctt ggttgtaggt gaccgggtta 360
ttgatgtggg atctgaatgg cgaactttca gcaatgacaa agcaacaaaa gatccatctc 420
gagttggaga ttctcagaat cctcttctga gtgatggaga tttgtctacc atgattggca 480
agggcacagg agctgcaagt tttgacgaat ttggcaattc taagtaccag aatcggagaa 540
caatgagcag ttctgatcgg gcaatgatga atgcattcaa agaaatcact accatggcag 600
acagaatcaa tctacctoga aatatagttg atcgaacaaa taatttatc aagcaagtat 660
atgaacagaa gagcctgaag ggaagagcta atgatgctat agcttctgct tgtctctata 720
ttgcctgtag acaagaaggg gttcctagga catttaaaga aatatgtgcc gtatcacgaa 780
tttctaagaa agaaattggt cgggtgttta aacttatttt gaaagcgcta gaaaccagt 840
tggtattgat tacaactggg gacttcatgt ccaggttctg ttccaacctt tgtcttcta 900
aacaagtaca gatggcagct acacatatag cccgtaaagc tgtggaattg gacttggttc 960
ctgggaggag ccccatctct gtggcagcgg cagctattta catggcctca caggcatcag 1020
ctgaaaagag gacccaaaaa gaaattggag atattgctgg tgttgctgat gttacaatca 1080
gacagtccta tagactgatc tatcctcgag cccagatct gtttctaca gacttcaaat 1140
ttgacacccc agtggaacaa ctaccacagc tataaattga ggcagctaac gtcaaatct 1200
tgaatacaaa actttgcctg ttgtacatag cctatacaaa atgtcgggtt gagcctttca 1260
tgaggaaaaa caaaagacat ggtacgcatt ccagggtgta atactattgc ttggcattct 1320
gtatgtatat actagtgaat catatttaat gatttaaat tcttatcaaa tttcttttgt 1380

```

```

agcaatctag gaaactgtat ttggaagat atttgaaatt atgtaattct tgaataaaac 1440
atTTTTcaaa actcaagttt ttgttatatg ttacatgtaa cttatgatac ataattacaa 1500
ataatgcaaa tcattgcagc taataaagct gatagacttt atttccatta cttatatata 1560
catagttttt tattttaata aatttatgga aagagcaaaa gcttttgaga accattgtta 1620
acatcaacat catagtttcc agtttgaaag gatgtgtatg tgagatttat tatgtatatt 1680
attaacaag aagtgatgag cttggccttg aaaggcacca gcttgagaga cattaataatg 1740
ttctaagtaa aaaaa 1755

```

<210> 282

<211> 1093

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (90)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (970)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1081)

<223> n equals a,t,g, or c

<400> 282

```

cccttcttgg ttgcgcgccc gtctctcgcg ttcttggyt gccagcccc gagggccgca 60
gcctccgcgg atccgggccc gctcggcccn tcccatggaa ggtgctcggg tcttcggggc 120
actgggtccc atcgggtccc cctcacctgg gctcaccctc gggggctctg ccgtgagcga 180
gcaccggctc agcaacaagc tgctggcttg gagcggcgtc ctcgagtggc aggagaagcg 240
cagaccctac tctgactcca ctgcaaagct gaagcggacc ctgccctgcc aagcctacgt 300
gaaccaaggc gagaacctgg agaccgacca gtggccgcag aagctgatca tgcagctgat 360
ccctcagcag ctgctgacca ccctgggccc cctgttccgg aactcccagt tggcacagtt 420
ccacttcacc aacagagact gcgactcgct caaggggctc tgccgcacatc tgggcaacgg 480
cttcgcgggc tgcatgctgt tccccacat ctccccctgt gaggtgcgcg tgctcatgct 540
cctgtactcg tccaagaaga agatcttcat gggcctcatc ccctacgacc agagcggcctt 600
cgtcagtgcc atccggcagg tcatcaccac ccgcaagcag gcagtgggac ctggtggtgt 660
caactcaggc ccagtccaga tcgtcaacaa caagtttctg gcattggagt gtgtcatgga 720
gtggcaggag cccaggcctg agcccaacag tcggtccaag aggtggctgc catcccacgt 780
ctacgtgaac cagggggaga tcctgaggac cgagcagtgg ccaaggaagc tgtacatgca 840
gtcatccccg cagcagctgc tgaccaccct agtgccgctg ttccggaaact cgcgcctggt 900
ccagttccac ttaccaagg acctggagac actgaagagc ctgtgccgga tcatggacaa 960
tggtctcgcn ggctgcgtgc acttttccta caaagcatcg tgtgagatcc gcgtgcttat 1020
gtcctgttac tcttcagaga agaaaatytt cattggcytc atcccccatg accagggcaa 1080
ntttgtcaa agg 1093

```

<210> 283

<211> 1556



<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1324)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1339)  
<223> n equals a,t,g, or c

<400> 283  
ggcacgaggg gaatcctcca cgtggctgtc ccagcacgag gaacccatgc acagtgtgtc 60  
agaaactgga cagttccgga cagcggwcaa ggcaaggawg tcatgcttga aggccagggt 120  
agacttgaga gagttcacat tccactgtca gcaccagcct cagcaactgt gcagagacct 180  
acaggcccac agccagtggc ctgtccgcat tgccctgtgc ccacaagcaa cagtccacag 240  
cccttggtgg cttctgttcc ttgtcccctc ggcttctctt cgcagccatc aggactaggt 300  
ttgtgcagga aggtgatgcc cactggaact ctccctcacac ctggcagctt catggatgtt 360  
gtatctgaac taaggaccag aggtgccag atgtttctgg ctctcacgt gtccttcagg 420  
acagaacaga agcacaaga ctcagccaag agttctcttt attcccttg atcctcccc 480  
aaggtgaggg cttaggcagc tgtagaacct caggaaagaa cggaatccag gcaatctgtt 540  
tagagacccc ccaactccaaa tttatccttt tcctttcctt cccctaagat gtttccaggg 600  
ccctctggtg cccacactgt cctcttcctt ccacttgggg gtggggaaat ccttcctgcg 660  
aggtcagggc atttctctac aaagtggcct gaatgaggcc aggccctgag aaggagccac 720  
cagctggagg aaaggggctc caagccttgc ttttaacacc cctgcaaaac cccaccctc 780  
ccaagatgtt cacaaaaggt gagaaattca ggtacgaaac catcaatgga caacttgaaa 840  
atgcatgttc ctccagccta tgcagttccc agagactctt gacaccggtc tctgtgtagg 900  
ctccagcct cagtttcccc cacagcagca cgggccccac tgtgtgtgtc ttcagggtccc 960  
cacagccctg cctttggttc ctggacattt ggtattctgc cctccactct ggtactatca 1020  
gagttagggc ggctctggat taaagctttt agccggtcta aagctacttt cttcaaagac 1080  
agtgggagga gaggttgctg gggcatcagc cctgttctcc acagctcctt aggcaagagc 1140  
ttaccagca gctgtgagca ccaagctggc cagcagaggc tgggggagga ctttcaggcc 1200  
aacacctgcc ccagctgagt ttgggactgt ccttaagcga ggtctggaga gaggcagcgg 1260  
cagcagccgg acggggagca ggccaagccg gaaccacagc ctgcaggtgt ggggtgttgt 1320  
catntgctga gatgccagng caccagcaag ggggatatgt tggcagtgat gtctggcttc 1380  
ggaggggtaca gtcctggctc ccagacaagg ggcggggaga acactgtgtc cttccagagg 1440  
ctgtaccaca ctcccactgc tgtcaccctt cactgaagcc tcgagcctcg gtagggcctc 1500  
cctcttctcc ctgtcctatc aagacttaca gcaagggtccc aggttgacag ggagac 1556

<210> 284  
<211> 1029  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (828)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (958)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (972)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (976)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (987)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1007)  
<223> n equals a,t,g, or c

<400> 284  
tgatggtgtg gtccaatgag cgggtcatgg gttgggtgtc cgggctgggc tgaaggaatt 60  
tgccacgaac ctacaggaga gcgggggtaca cggggcactg ctgcacctgg acgagacctt 120  
cgactactcc gacctggcct tgetcctgca gatccccacg cagaatgcac aggcccgga 180  
gcttctggag aaggaattca gcaaccttat ctcttaggc acagacaggc ggctggacga 240  
ggacagcgcc aagtctttca gccgctcccc atcctggcgg aagatgttcc gggagaagga 300  
cctccgaggc gtaactcccc actcagctga gatgttgccc cccaactttc gttcggctgc 360  
agcgggagcc ctgggctctc cggggctccc tctccgcaag ctgcagccag aaggccagac 420  
ttctgggagt tcccgggcag acggcgtttc ggtccggacc tattcctgct agtgcaggcc 480  
tccaggtgac ctcaactcga cggaagaatc ttcccaggc tgggctgttc cctctcctgc 540  
ccggactgtg gcctcgccgg ggagagcggg cgggggagct cgcgccgagg actggaccat 600  
ctgtacagac cagcgggagt gcgcgcgccc gcctcgaca gggccggggc tggaccaaac 660  
cacatgaact ggactgagag ggggaagaag cggggaggaa gaaatcccgc cccaaacgtc 720  
cgctttcctt ttctctactt tgtaatttat tgatcagttt ctgttgggag acgggtgtcc 780  
tttaccgcg ggaagggggc ggggcttccc tcccgggccg catgcggnga gargctgctc 840  
cctccctttt ttctgccc gtcgcggggc ccaagtcttt ccttcttcgt ccgaaaggag 900  
gggaggggga ctctgtctac aagcctcgcc ccctgtgcca ctcagtccga cccgccngt 960  
tccggttcgc cnggtncccc cgggttnatc tggcggggcg ggtcccnttg tgccttcccc 1020  
ccgtgtttt 1029

<210> 285  
<211> 1583  
<212> DNA  
<213> Homo sapiens

<220>

<221> misc feature  
<222> (1411)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1531)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1557)  
<223> n equals a,t,g, or c

<400> 285  
tgtgtctgcy ttgaggggtgt tgaggggtcca cgctgtgaca agtgcacgcg aggggtactcg 60  
gggggtcttcc ctgactgcac accctgccac cagtgccttg ctctctggga tgtgatcatt 120  
gccgagctga ccaacaggac acacagattc ctggagaaaag ccaaggcctt gaagatcagt 180  
ggtgtgatcg ggccttaccg tgagactgtg gactcgggtg agaggaaagt cagcgagata 240  
aaagacatcc tggcgagag ccccgagca gagccactga aaaacattgg gaatctcttt 300  
gaggaagcag agaaactgat taaagatggt acagaaatga tggctcaagt agaagtgaaa 360  
ttatctgaca caacttccca aagcaacagc acagccaaag aactggattc tctacagaca 420  
gaagccgaaa gcctagacaa cactgtgaaa gaacttgctg aacaactgga atttatcaaa 480  
aactcagata ttcgggggtgc cttggatagc attaccaagt atttcagat gtctcttgag 540  
gcagaggaga ggggtgaatgc ctccaccaca gaaccaaca gcaactgtgga gcagtcagcc 600  
ctcatgagag acagagtaga agacgtgatg atggagcgag aatcccagtt caaggaaaaa 660  
caagaggagc aggtcgcct ccttgatgaa ctggcaggca agctacaaag cctagacctt 720  
tcagccgstg ccgaaatgac ctgtggaaca cccccagggg cytcctgtty cgagaytgaa 780  
tgtggcgggc caaactgcag aactgacgaa ggagagagga agtgtggggg gcctggctgt 840  
ggtggtctgg ttactgttg acacaacgcc tggcagaaaag ccatggactt ggaccaagat 900  
gtcctgagtg ccctggctga agtggaacag ctctccaaga tggctcttga agcaaaactg 960  
agggcagatg agggcaaaaca aagtgtgtga gacattctgt tgaagacaaa tgctacaaa 1020  
gaaaaaatgg acaagagcaa tgaggagctg agaaatctaa tcaagcaaat cagaaacttt 1080  
ttgaccagg atagtgtctga tttggacagc attgaagcag ttgctaata agtattgaaa 1140  
atggagatgc ctgacacccc acagcagtta cagaacttga cagaagatat acgtgaacga 1200  
gttgaaagcc tttctcaagt agaggttatt cttcagcata gtgctgctga cattgccaga 1260  
gctgagatgt tggtagaaga agctaaaaga gcaagcaaaa gtgcaacaga tgttaaagtc 1320  
actgcagata tggtaaagga agctctggaa gaagcagaaa agggccagggt cgcagcagag 1380  
aaggcaatta aacaagcaga tgaagacatt ncaaggaaacc cagaacctgy taacttccsa 1440  
ttggagtctt kgaaacagca gctttctgga ggaaaccttg ttcaacgcgt tcccagggca 1500  
tccagcgagt ttagagagga tgtgggaaga nctttaagcg gaaagctggc ccaaaanccc 1560  
gggggaggcc gaattttttg gaa 1583

<210> 286  
<211> 1177  
<212> DNA  
<213> Homo sapiens

<400> 286  
gctcaaaatg tttaaccaatg ttttaagatg tctttatcaa gcaaccgtat cagcagagaa 60  
aagayatctc aaaatgttta ccaatgtttt aagaagcttt gtgtgatatt cttccaaatg 120

```

tagttaccaa atataatatg gtagaaaagg ctaaatacata cttaatgagc aaattgaagt 180
aagcttttaa agtatatttc tcttttggtg aaaggccaat ggagacattg tgaatttaag 240
tgaacatttg cctcaagatg ttaactataa acacactgca tacaattttc ttctgaataa 300
caaatgaatg cttattgctg catgatgtaa gcaaaaagtc ttatttttcc tattcatttg 360
aaataagtta tggcttaaaa tgcttttgga gtttatttct caaaattaaa atctgggcac 420
atgagcttta gtttgttttc tggtttaaaa aataaaaagg tttctcttaa cagtatttcc 480
agtgacaatg caaggtaagt atatcaaagg aaatcaacag ttgtgcttg gggctttttg 540
ttatgggata ttgatttctt gtttttttcc cgtaacattg tctgctgcaa tttaaataaa 600
aattacgaca ttttaagata tttcatagac aaaccaaaca aaaatatatg tttttacttt 660
aaagtgaatg tttttctctt cagctgatct aaaaatgaaa gcaaratatc ttatgtagaa 720
atattttgat aatattttta cagtgaagct tcccattgtt ttatgtctta agtttctttg 780
ctgctgttat gtaggttgca caagaacttt tactcacttg taattgtgcc tcagactttt 840
tgaaagtcta cttctataat tgccccgacg atctagattc tacatgttac cattgggtta 900
ttcttggtct ttctgtattt aaaacttttg ctgtactaag caaatgcaag gttataattt 960
agctaatagt agtttacaga caattctgat gattatgatt tcatttggtt taactaagct 1020
gtactagttc atttcataag gaaatgatac tgtagacaaa tgtaataaaa gcctgtgagt 1080
caagcatcaa gtggtgtttg ttagaaataa actagagatt tttaaaaaaa aaaaaaaaaa 1140
aaaaaaaaaa aaaaaaaaaa acccccgggg gggggccc 1177

```

<210> 287

<211> 506

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (394)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (470)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (481)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (494)

<223> n equals a,t,g, or c

<400> 287

```

acaagtagct gcagtacggt acggaattac agggtagacc caagcgtacg taaaatttaa 60
aaacaaagga ctatttataa atacagttta ttaacaaacg tgaactactt tctgttacat 120
taggtgttcc ctagtgtttc ttaatttctt tttagaaagt gtatttttat tagtattttt 180
ccggtgaaca gaagatttgt ttggatttaa acatttacta agacagtacc tattaggaaa 240
accaaataat gcaaatggtc aattcgattt taatttctca aaagatactc tggtatccag 300
aagattaaaa tgcctacatt gagtgcttaa aaaaaaaaaa acmactgtga tratktgagc 360

```

223

```

agaatggcca gtaagttaag ccttttttga tccnggtaat ccagggtatc catttaccat 420
ggaaagggga ttccccaac tactggcca gagggaggtt tggtttttn aaatttaagg 480
nggggaaatt ttanccctat aaaatt 506

```

```

<210> 288
<211> 948
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (3)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (926)
<223> n equals a,t,g, or c

```

```

<400> 288
ttnggccgag cttgggtcat ggcgccgccc ggcgcgctgc tggatgagg cgtgagcggc 60
tcggggaaat ccaccgtggg cgccctgctg gcatctgagc tgggatggaa attctatgat 120
gctgatgatt atcacccgga ggaaaatcga aggaagatgg gaaaaggcat accgctcaat 180
gaccaggacc ggattccatg gctctgtaac ttgcatgaca ttttactaag agatgtagcc 240
tcgggacagc gtgtggttct agcctgttca gccctgaaga aaacgtacag agacatatta 300
acacaaggaa aagatggtgt agctctgaag tgtgaggagt cgggaaagga agcaaagcag 360
gctgagatgc agtcctggt ggtccatctg agcgggtcgt ttgaggtcat ctctggacgc 420
ttactcaaaa gagagggaca ttttatgccc cctgaattat tgcagtcca gtttgagact 480
ctggagcccc cagcagctcc agaaaacttt atccaaataa gtgtggacaa aaatgtttca 540
gagataattg ctacaattat ggaaacccta aaaatgaaat gacaatgatt ttgtatcagt 600
ggtccaaaca gaactaagca taaatcattg tgccatccca aacctcggtc cagccgcctt 660
gcccatacta gattctaaat gtttctaaa gcaaacccca atgtgtcaag acagacttgt 720
ttaggtgtaa ttttaggaat tatgtggtt catcaggaag cagaggggga gttttaaaag 780
tcaagcttaa attgaagttt aaattcatct ataaccaaat caaatgatca gaggaaattc 840
tgtaatcaat gctggaaatc gttacattgt ttagaacatt cttgctcatg cctgtatttg 900
cacaaataaa tgaaacttcg ctgtcnaaaa aaaaaaaaa aaaaaaaaa 948

```

```

<210> 289
<211> 1034
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (376)
<223> n equals a,t,g, or c

```

```

<400> 289
ggcacgagct cgtgccggtt tgacctggag catgggtcct ggaccaaatt gccccgcagc 60
ctgcgcagta gggataagag ggcagacttt gtggttgggt cccttggggg ccacattgtg 120
gccattgggg gccttggaag ccagccatgt cctttgggct ctgtggagag ctttagcctt 180

```

```

gcacggcggc gctgggaggc attgcctgcc atgcccactg cccgctgctc ctgctctagt 240
ctgcaggctg ggccccggct gtttggttatt gggggtgtgg cccagggccc cagtcaagcc 300
gtggaggcac tgtgtctgcg tgatggggtc tgaaggcttg gtgggagctg tccactggag 360
cagctcattg ccagangmrg ctatttctat ggctcctttt gctgctgagg aactcactg 420
tggctctgtg ggatgagaga ggcattgggg tgagcacttg aaacactgcc ttggggcctt 480
gggttagggg agcctttgtc tttagtgcag gacacacata tgcttacacc tacctttatc 540
accattcggt catgaatcat gcctagctcc atccttgccc tgggacctac taggccttcc 600
atccaactgg gaaatgggga gaagcaaagc tggcctcatg ctcttcaggg tcagttccta 660
tctggagttg accaggccta cccagttgc cattcctgaa aaatctcagc tgccaggctg 720
cctttagggt ccctgtagac ccaggagagt tgagagggtg ggggacacag agagaataga 780
gaggatgttg gaactgccag agggccggag cgcaggagtt caagtggagg aatgctggct 840
ttgagccctc tacactgctg gttgtatgac cttggacaag tcacttcacc tctctgtgcc 900
tcagcatcct catctataaa tgggatctc tgaaaccttc ctaccctacc tacctcacag 960
ggctgttgtg aggaccagg gagtttggat gtggaagtaa aagtgtgtgt aaaacctaaa 1020
aaaaaaaaaa aaaa 1034

```

<210> 290

<211> 3091

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (24)

<223> n equals a,t,g, or c

<400> 290

```

cccagtagct cgtgccgctc gtgnccgcc aactctcagtt tgatcttaaa gtctgaataa 60
taaaacaaat cccagcagta atacatttct taaacctcac agtgcagat atacttttct 120
attctgatcc tgtgtttgca aaaatataca catgtatatc atagttcctc actttttatt 180
catttgtttt cctattacct gtagtaaata tattagttag tacatggaat ttatagcatc 240
agctaccccc aggaacagca cctgacaggc gggggatttt ttttcaagtt gttctacatt 300
tgcataaatt atttctatta ttattcatgt atgttattta tttctgaatc acactagtcc 360
tgtgaaagta caactgcaag gcagaaagtg ttaggatttt gcatctaattg ttcattatca 420
tgggtattgat ggacctaaag aaataaaaaat tagactaagc ccccaaataa gctgcatgca 480
tttgtaacay gattagtaga ttgaaatata tagatgtagt attttgggta tctagggtgt 540
ttatcattat gtaaagggaat taaagtaaag gactttgtag ttgtttttat taaatatgca 600
tatagtagag tgcaaaaata tagcaaaaat aaaaactaaa ggtagaaaag cattttagat 660
atgccttaat ttagaaactg tgccagggtg ccctcggaat agatgccagg cagagaccag 720
tgccctgggtg gtgcctcctc ttgtctgccc tcatgaagaa gcttccctca cgtgatgtag 780
tgccctcgta ggtgtcatgt ggagtagtgg gaacaggcag tactgttgag aggagagcag 840
tgtgagagtt tttctgtaga agcagaactg tcagcttggt ccttgaggct tccagaacgt 900
gtcagatgga gaagtccaag ttccatgct tcaggcaact tagctgtgta cagaagcaat 960
ccagtgtggt aataaaaagc aaggattgcc tgtataattt attataaaat aaaagggatt 1020
ttaacaacca acaattccca acacctcaaa agcttggtgc attttttggg atttgagggt 1080
tttatctgaa ggttaaaggg caagtgtttg gtatagaaga gcagtatgtg ttaagaaaag 1140
aaaaatattg gttcgcgtag agtgcaaat agaactagaa agttttatc gattatcatt 1200
ttgagatgtg ttaaagtagg tttcactgt aaaatgtatt agtgtttctg cattgccata 1260
ggccctgggt aaaaactttc cttaggtttc aggaagactg tcacatacag taagcctttt 1320
tccttctgac ttataataga aaatgttttg aaagtaaaaa aaaaaaaatc taatttggaa 1380
atttgacttg ttagtttctg tgtttgaaat catggttcta gaaatgtaga aattgtgtat 1440

```

```

atcagatact catctaggct gtgtgaacca gcccagatg accaacaatcc ccacacctct 1500
acatctctgt cccctgtatc tcttcctttc taccactaaa gtgttccttg ctaccatcct 1560
ggcttgtcca catgggtgctc tccatcttcc tccacatcat ggaccacagg tgtgcctgtc 1620
taggcctggc caccactccc aacttgacct agccacattc atctagagat ggttcctgat 1680
gctgggcaca gactgtgctc atggcaccca ttagaaatgc ctctagcatc tttgtatgca 1740
tcttgatttt taaaccaagt cattgtacag agcattcagt tttggctgtg gtaccaagag 1800
aaaaactaat caagaatata aaccacattc caggctgctg ttttctctcc atctacaggc 1860
cacactttta ctgtatttct tcatacttga aattcattct gctattttca tatcagggta 1920
cagacttata aggggtgcatg ttccttaaag gtgcataatt attcttattc cgtttgctta 1980
tattgtctaca gaatgctctg ttttgggtgt ttgagttctg cagacccaag aagcagtgtg 2040
gaaattcact gcctgggaca cagtcttata agaagtgttg cagggtgactt tgtatcagat 2100
gttgcttctc ttttctctgt acacagattg agagttacca cagtggcctg tcgggtccac 2160
cctgtgggtg cagcacagct ctctgaaagc aagaaccttc ctacctattc taacgttttt 2220
gcccctctaag aaaaatggcc tcagggtatgg tatagacata gcaagagggg aagggtctgtc 2280
tcactctagc aaccatccct ccattacaca cagaaagccc tcttgaagca aaagaagaag 2340
aaagaagaa agcttatctc taaggctact gtcttcagaa tgctctgagc tgaatgctct 2400
tgctcctttc ccaagaggca gatgaaaata tagccagttt atctataccc ttcctatctg 2460
aggaggagaa tagaaaagta gggtaaatat gtaacgtaaa atatgtcatt caaggaccac 2520
caaaacttta agtaccctat cattaaaaat ctggttttaa aagtagctca agtaagggat 2580
gctttgtgac ccagggtttc tgaagtcaga tagccattct tacctgcccc ttactctgac 2640
ttattgggaa agggagaact gcagtggtgt ttctgttgca gtggcaaagg taacatgtca 2700
gaaaattcag agggttgcat accaataatc ctttggaaac tggatgtctt actgggtgct 2760
agaatgaaaa ttaggtattt tattgtcaga tgatgaagtt cattgttttt ttcaaaattg 2820
gtgttgaaat atcactgtcc aatgtgttca cttatgtgaa agctaaattg aatgaggcaa 2880
aaagagcaaa tagtttgtat atttgttaata ctttttgtat ttcttacaat aaaaatattg 2940
gtagcaataa aaaataataa aaacaataac tttaaactgc tttctggaga tgaattactc 3000
tcctggctat tttctttttt actttaatgt aaaatgagta taactgtagt gagtaaaatt 3060
cattaaattc caagttttag caaaaaaaaaa a                                     3091

```

&lt;210&gt; 291

&lt;211&gt; 518

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 291

```

aggcatgaag aagagtgtgg gtactgtttc ctccacagcg gccagagtca ggggtggggag 60
tgagtccagt tgagggggaa acagtaccag cactgcgggg catgaagaag agtgtggggc 120
tgccggtggc cgtgcagtggt gtggctctgc cctggcaaga agagtttgtt ctgcggttca 180
tgcgggaggt ggagcgactg atgacctctg aaaagcagtc atcctgatgg ctctggctcc 240
agaggacctg agactcacac tctctgcagc ccagcctagt cagggcacag ctgccctgct 300
gccacagcaa ggaaatgtcc tgcatggggc agaggcttcc gtgtcctctc ccccaacccc 360
ctgcaagaag cgccgactcc ctgagtctgg acctccatcc ctgctctggt cccctctctt 420
cgctctgatc cctccacccc catgtggcag cccatgggta tgacatagcc aaggcccaac 480
taacagtcaa gaaacaaaaa aaaaaaaaaa aaaaattc                                     518

```

&lt;210&gt; 292

&lt;211&gt; 498

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

<221> misc feature  
 <222> (447)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (468)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (475)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (479)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (482)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (489)  
 <223> n equals a,t,g, or c

<400> 292  
 ctcgtgccg attcggcacg agcaacgtcg ctccagctgc tcttgacgac tccacagata 60  
 ccccgaaagcc atggcaagca agggcttgca ggacctgaag caacaggtgg aggggaccgc 120  
 ccaggaaagcc gtgtcagcgg ccggagcggc agctcagcaa gtggtggacc aggccacaga 180  
 ggcggggcag aaagccatgg accagctggc caagaccacc caggaaacca tcgacaagac 240  
 tgctaaccag gcctctgaca ccttctctgg gatcgggaaa aaattcggcc tctgaaatg 300  
 acagcaggga gacttgggtc ggctctctga aatgayagca gggagacttg ggtgaccccc 360  
 cttccaggcg ccatctagca cagcctggcc ctgatctccg ggcagccacc acctcctcgg 420  
 tctgccccct cattaaaatt cacgttncca aaaaaaaaaa raaagggngg ccgcntagn 480  
 gntccaagnt tagttacg 498

<210> 293  
 <211> 469  
 <212> DNA  
 <213> Homo sapiens

<400> 293  
 ggccagccct ggggcgcctt aaaaaccgga gctggcgctt ggcakcgcca ctctgggcag 60  
 gatccaacgt cgctccagct gctcttgacg actccacaga taccgccgaag ccatggcaag 120  
 caagggcttg caggacctga agcaacaggt ggaggggacc gccaggaag ccgccatgga 180  
 ccagctggcc aagaccacc aggaaccat cgacaagact gctaaccagg cctctgacac 240  
 cttctctggg atygggaaaa aattcgcct cctgaaatga cagcaggag acttgggtcg 300



227

```
gcctcctgaa atgayagcag ggagacttgg gtgaccccc ttccaggcgc catctagcac 360
agcctggccc tgatctccgg gcagccacca cctcctcggg ctgccccctc attaaaattc 420
acgttcccaa aaaaaaaaaa aaaaaaaaaa gggggggccc gtccccatt 469
```

&lt;210&gt; 294

&lt;211&gt; 668

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (568)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (650)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (652)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (658)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 294

```
gcacagaagg gggaggccaa agtgggtggg agcgcgtgct gttgggagtt gcttggaggt 60
tgccggcgcg gggctgaagg ctagcaaacc gagcgatcat gtcgcacaaa caaatttact 120
attcggacaa atacgacgac gaggagttag agtatcgaca tgatcatgctg cccaaggaca 180
tagccaagct ggtccctaaa acccatctga tgtctgaatc tgaatggagg aatcttggcg 240
ttcagcagag tcagggatgg gtccattata tgatccatga accagaacct cacatcttgc 300
tgttccggcg cccactacct aagaaaccaa agaaatgaag ctggcaagct acttttcagc 360
ctcaagcttt acacagctgt ctttacttcc taacatcttt ctgataacat tattatgttg 420
ccttcttggg tctcactttg atatttaaaa gatgttcaat acactgtttg aatgtgctgg 480
taactgcttt gcttcttgag tagagccacc accaccatag cccagccaga tgagtgtctt 540
gtggaccaca gcctaagctg agtgtgancc cagaagccac gatgtgctct gtatccagac 600
acacttggca gatggaggaa gcactctgatt gagacatggt gtacaggtcn gnaatgcngt 660
ttgttttc 668
```

&lt;210&gt; 295

&lt;211&gt; 1400

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 295

```
gctttgtcct ccagtggctg gtaggcagtg gctgggaggc agcggcccaa ttagtgtcgt 60
gcggcccgtg gcgaggcgag gtccggggag cgagcgagca agcaaggcgg gagggggtggc 120
```

```
cggagctgcg gcggctggca caggaggagg agcccgggcg ggcgaggggc ggccggagag 180
cgccagggcc tgagctgccg gagcgggccc tgtgagttag tgcagaaagc aggcgcccgc 240
gcgctagccg tggcaggagc agcccgcacg ccgcgctctc tccctgggcg acctgcagtt 300
tgcaatatga ctttggagga attctcggct ggagagcaga agaccgaaag gatggataag 360
gtgggggatg ccctggagga agtgctcagc aaagccctga gtcagcgcac gatcactgtc 420
ggggtgtacg aagcggccaa gctgctcaac gtcgaccccg ataactggtt gttgtgcctg 480
ytggcgggcg acgaggacga cgacagagat gtggctctgc agatccactt caccctgac 540
caggcgtttt gctgcgagaa cgacatcaac atcctgcgcg tcacaacccg ggccggctgg 600
cggastcctg ctcttgagga ccgacgctgg ccccgcgggc agcgagggcg ccgagcagcc 660
cccgacctg cactgctgtt ggtgacgaat ccacattcat ctcaatggaa ggatcctgcc 720
ttaagtcaac ttatttgttt ttgccgggaa agtcgctaca tggatcaatg ggtccagtg 780
attaatctcc ctgaacggtg atggcatctg aatgaaaata actgaaccaa attgcaactga 840
agtttttgaa atacctttgt agttactcaa gcagttactc cctacactga tgcaaggatt 900
acagaaactg atgccaaggg gctgagttag ttcaactaca tgttctgggg gcccgagat 960
agatgacttt gcagatggaa agaggtgaaa atgaagaagg aagctgtgtt gaaacagaaa 1020
aataagtcaa aaggaacaaa aattacaaag aaccatgcag gaaggaaaac tatgtattaa 1080
tttagaatgg ttgagttaca ttaaaataaa ccaaatatgt taaagttaa gtgtgcagcc 1140
atagtttggg tatttttggg ttatatgccc tcaagtaaaa gaaaagccga aagggttaat 1200
catatttgaa aaccatattt tattgtattt tgatgagata ttaaattctc aaagttttat 1260
tataaattct actaagtatt tttatgacat gaaaagtatt ttatgctata aattttttga 1320
aacacaatac ctacaataaa ctggtatgaa taattgcatc aaaaaaaaaa aagggggggc 1380
gctcgcgatc tagaaactag 1400
```

<210> 296

<211> 960

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (599)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (859)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (933)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (950)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (951)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (959)

<223> n equals a,t,g, or c

<400> 296

```
gtcagcccga gcccggtgcr ggcctttaag ggccgggggc gtgtagcggg cccgccccct 60
ccccgcggcg cccgcagtcg gttaagtgcg agccccggcg caggggcccg atctggcccg 120
gggcccggcg cgggtgtgga gcggcgcgtc atgtacacca tcaccaaggg gccagcaag 180
ctggtcgcgc agcgccgcac aggtcccacg cagcagcagg tggaggggcg gctcggcgag 240
ctcctgaaat gccggcagcc cgcgcgcgcg acctcgcagc ccccgcgggc gcagccytth 300
gcgcascgcc gggacccttg cccctgtcga gtccagggcc aaggcttggt ttcaatcgtg 360
tgaatggccg gcgggccccc tccacgtccc catccttcga ggggaccag gagacctaca 420
cagtggccca cgaggagaat gtccgctttg tgtccgaagc ctggcagcag gtgcaacagc 480
agctggatgg tggcccagcc ggtgagggcg ggccaaggcc tgtgcagtag gtggagagga 540
cccccaatcc cgggtgcag aactttgtgc ccattgacct agacgagtgg tgggcgcanc 600
agttcctggc gagaatcacc agctgttcct agtggctgct gggagggggc gctgctacac 660
ggccgacctg tcgccaggag agaagcatgg cgccctgcc acccactgcg cctggctggg 720
tgccggccac acctgaagtg ccagcatttg gacttttgca ccttttttcc ccttgggccc 780
gctgtcccaa ccaagctgcc atgccaaggg ccgaaccctg ctgacctcag cctgctcac 840
tgtgcccagg gaccagcna caccctggg gctggcaggg aggagctcca ggctaataaa 900
gtggagaaac tgtcaaaaaa aaaaaaaaaa aanctcgagg gggggcccgn nccaattnc 960
```

<210> 297

<211> 657

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (29)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (86)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (88)

<223> n equals a,t,g, or c

<400> 297

```
caaaagctgg agctccaccg cggtagcgn cgccttagaa ctagtggatc cccggggctg 60
caggaattcg gcacgagctc gtgccngncc tttggagcag agaggaggca atggccacca 120
tggaagaaca ggtgatctgc gccctgggtc tgggtgtccat gctggccctc ggaccctgg 180
ccgaggccca gacagagacg tgtacagtgg ccccccgtga aagacagaat tgtggttttc 240
ctggtgtcac gccctccagc tgtgcaaata agggctgctg ttctgacgac accgttcgtg 300
```

```

gggtcccctg gtgcttctat cctaatacca tcgacgtccc tccagaagag gagtgtgaat 360
tttagacact tctgcaggga tctgcctgca tcctgacgcg gtgccgtccc cagcacgggtg 420
attagtccca gagctcggct gccacctcca ccggacacct cagacacgct tctgcagctg 480
tgccctcggt cacaacacag attgactgct ctgactttga ctactcaaaa ttggcctaaa 540
aattaaaaga gatcgatatt aaaaaaaaaa gaaaaggaaa aaaaagggag gccgtctaag 600
aggatccaag cttacgtaac gcgtgcatgc gaaggtcata gctcttctat agtgtca 657

```

<210> 298

<211> 892

<212> DNA

<213> Homo sapiens

<400> 298

```

gcagccaggc tctcaggga ggtccatgct gcttggcctg agttcaaggc tttctgcctg 60
tagcctggac tcccgtggac ccccgtaggc aggtggcttc cccgtggcat ctccacaccg 120
cctctgcctg cccctgtgga ctgatgctat cgcgcaccgt cccacgaccc caccocgagc 180
tcctgaagcc ggggtctgag cctgcatcac ctctggcctc tcatccccc cttctcctgag 240
agcagtggtc acagcgccg gccgctctgc tgagaaggca gagaggcagg ctcaggcctc 300
agcgtggaca gcagggataa ggggcacgaa ggacggggac tcggcccctt cagaattcct 360
caggactctc aggtgcagct ttgccaaaaa ggaacttttc atgtcatgca gttgagggga 420
cttagtctca atcccaggct cctcttgact ctgggcagct ttaatcaggc tgggcagcct 480
ctgctacagc gtggagtggg atggctctct tccctcagcc acgccgcttg tgaggacaga 540
ggtgggggag tgggaagtgg gaagtcacca gagaacagga gagggatttg agggcgcgac 600
cccagcgctc tccacggacc agccagaggg actggagcca ggtgtgcatg ggttcaaggc 660
cctggccctg cccagcctct gtcttgggag ctcagcccca gggttcgggc gtcagcagtt 720
tccaagaac aagatgtgat ggcatctgct gctgaaaccc tgatagggac caggccccct 780
gcaccgctgt cagcctgagg aattaaagct ttggtgctgg gaaragcaaa aaaaaaaaaa 840
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa tc 892

```

<210> 299

<211> 1624

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1621)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1623)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1624)

<223> n equals a,t,g, or c

<400> 299

```

cccggtgctc aggaattcgg cagagagag gaggtccac aggtcctgc cctgggctac 60

```

```

cgagtccccc gatggtgtta tacattaaat atccaggatg gagaagccac atgctactca 120
ccgaaggagg aaattatcac agcagcctgg gcacgcgttg tgagctctcc tgtgaccggg 180
gctttcgatt gattggaagg aggtcgggac aatgcctgcc aagccgtcgt tggctctggaa 240
ctgcctactg caggcagatg agatgccacg cactaccatt catcactagt ggcacttaca 300
cctgcacaaa tggagtgtct cttgactctc gctgtgacta cagctgttcc agtggctacc 360
acctggaagg tgatcgagc cgaatctgca tggaaagtgg gagatggagt ggaggcgagc 420
ctgtatgtgt agacatagat cccccaaga tccgctgtcc ccactcacgt gagaagatgg 480
cagagccaga gaaattgact gctcgagtat actgggaccc accgttggtg aaagattctg 540
ctgatggtac catcaccagg gtgacacttc ggggccctga gcctggctct cactttcccg 600
aaggagagca tgtgattcgt tacactgcct atgaccgagc ctacaaccgg gccagctgca 660
agttcattgt gaaagtacaa gtgagacgct gcccaactct gaaacctccg cagcacggct 720
acctcacctg cacctcagcg ggggacaact atggtgccac ctgtgaatac cactgtgatg 780
gcggttatga tcgccagggg acaccctccc gggctgtgca gtccagccgc cagtggtcag 840
gttcaccacc aatctgtgct cctatgaaga ttaacgtcaa cgtcaactca gctgctgggc 900
tcttgatca attctatgag aaacagcgac tcctcatcat ctcagctcct gatccttcca 960
accgatatta taaaatgcag atctctatgc tacagcaatc cacctgtgga ctggatttgc 1020
ggcatgtgac catcattgaa ctggtgggac agccacctca ggaggtgggg cgcacccggg 1080
agcaacagct gtcagccaac atcatcgagg agctcaggca atttcagcgc ctcactcgt 1140
cctacttcaa catggtgttg attgacaagc agggatttga ccgagaccgc tacatggaac 1200
ctgtcacccc cgaggaaatc ttcacattca ttgatgacta cctactgagc aatcaggagt 1260
tgaccacgcy tcgggagcaa agggacatat gcgagtgaac ttgagccagg gcatgggttaa 1320
agtcaaggga aaagctcctc tagttagctg aaactgggac ctaataaaaag gaggaatgt 1380
tttcccacag ttctagggac aggactctga ggtgggtgag tttgacaaat cctgcagtgt 1440
ttccaggcat ccttttagga ctgtgtaata gtttccttag aagctaggta gggactgagg 1500
acaggccttg ggcagtgggt tgggggtaga agttcttctt ttcctaaccg gggccctgc 1560
ccagctctcc aaagtctttc agaaaagtaa atcctaaatt cagtgatgaa aaaaaaaaaa 1620
nann
1624

```

<210> 300

<211> 1969

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (13)

<223> n equals a,t,g, or c

<400> 300

```

ttaatttagg tgnacactat agaagggtac gcctgcaggt taccggatcc ggaattcccg 60
ggatccggag ccgcccgaag ccggtgccgc agccccctgc gcccccggtg cccccgacat 120
gtccttccgc aaagtgttcc ggcagagcaa attccggcat gtgttcgggc agccggtcaa 180
gaacgaccag tgctatgagg acattcgcgt gtcccgtgtt acctgggaca gcaccttctg 240
cgccgtcaac cccaagttcc tggcgggtgat tgtggaggcc agtggagggg gtgcctttct 300
ggtgctcccc ctaagcaaga cgggccgcat tgacaaggcc taccgacggg tgtgtgggca 360
cacgggacct gtcctggaca tcgactggtg tcctcacaac gacgaatcat agccagcggy 420
tcggaggact gcacggtcat ggtgtggcag atcccagaga acgggctgac ctccccgctg 480
acagagccgg tgggtgtact ggaggggcac accaagcgag tgggcatcat cgcctggcac 540
cccacggccc gaaacgtgct gctcagtgca ggctgcgaca acgtggtaact catctggaat 600
gtgggcacag cggaggagct gtaccgcctg gacagcctgc accctgacct catctacaat 660
gtcagctgga accacaatgg cagcctgttt tgctcagcat gcaaggacaa gagcgtgcgc 720

```

```

atcatcgacc cccgtcgggg caccctggtg gcagagcggg agaaggctca tgagggggcc 780
cgggcccatgc gggccatctt cctggcagat ggcaagggtg tcaccacagg cttcagccga 840
atgagcgagc ggcagctggc gctctgggac ccagaaaacc tcgaggaacc catggccctg 900
caggaactgg actcgagcaa cggggccctg ctgcccttct acgaccccga caccagtgtg 960
gtctacgtct gcggcaaggg tgactccagc atccggtact ttgagatcac agaggagcct 1020
ccctacatcc acttcctgaa cacgttcacc agcaaggagc cgcagcgggg tatgggcagc 1080
atgcccgaagc ggggcctgga ggtagcaag tgcgagatcg cccggttcta caaactgcat 1140
gagcgcaagt gtgagcccat cgtcatgact gtgccaagaa agtcggacct cttccaggat 1200
gatctgtacc ccgacacagc cgggcccag gcagccctgg aggctgagga gtgggtgagc 1260
ggcggggatg ccgacccgat cctcatctca ctgcgggagg cctacgtgcc cagcaagcag 1320
cgggacctga agatcagccg gcgcaacgtg ttgtctgaca gccggcccgc catggccccg 1380
ggctcctccc acctaggggc ccccgctccc accaccactg ctgctgatgc cacccccagc 1440
ggcagcctgg ccagagccgg ggaggtggg aagctggagg aggtgatgca ggagctgcgg 1500
gccctgaggg agtgggtcaa ggagcagggc gaccgcatct gccgcctgga ggagcagctg 1560
ggccgcatgg agaacgggga tgcgtagggc cacagccaca cgccaccttc atctcctccg 1620
ccgccccctt cccactcagc ttctgccagc gggctgcacc gggctagctg gctgcccaga 1680
gcctctgagg cagcgcaggg gtcagtcccc acccccaccc gtcccaggcc caggccgaag 1740
ccagcgccca gctttcctca ctgttcctgt ggaggatgtc tacgcccagg cgagctcctc 1800
gacctctgag ggacctctc cccgaccact gccagccct ctgctccctc cccagaggag 1860
gcgggagggt gggctctata ttttcattcc aaataaaatt ctctttctaa aaaaaaaaaa 1920
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaacgga cgtcgtggg 1969

```

<210> 301

<211> 1882

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (22)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (223)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1840)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1849)

<223> n equals a,t,g, or c

<400> 301

```

ggagctctcg gcctcggtt tngacgacgg caacttctcg ctgctcatcc gcgcgggtgga 60
ggagacggag gcggggctgt acacctgcaa cctgcacat cactactgcc acctctacga 120
gagcctggcc gtccgcctgg aggtcaccga cggccccccg gcacccccgc ctactgggac 180

```

```

ggcgagaagg aggtgctggc ggtggcgcg cggcaccgct ytnctgacct gcgtgaaccg 240
cgggcacgtg tggaccgacc ggcacgtgga ggaggctcaa caggtggtgc actgggaccg 300
gcagccgccc ggggtcccg cgcaccgccc ggaccgcctg ctggacctct acgcgtcggc 360
gagcgccgcg ctacgggccc ctttttctgc cgamcgcggt gctgtgggag cggatgcctt 420
taagcgcggt gacttctcac tgcgtatcga gccgctggag gtcgcccagc agggcaccta 480
ctcctgccac ctgcaccacc attactggcg cgcggccaca acgtcatcaa tgtcatcgtc 540
cccagagacc gagcccactt cttccagcag ctgggctacg tctggccac gctgctgctc 600
ttcatcctgc tactggtcac tgcctcctg gccgcccga ggccgaggag gctacgaata 660
ctcggaccag aagtcgggaa agtcaaagg gaaggatgtt aacttggcgg agttcgctgt 720
ggctgcaggg gaccagatgc tttacaggag tgaggacatc cagctagatt acaaaaacaa 780
catcctgaag gagaggcg agctggccc cagccccctg cctgccaaat acatcgacct 840
agacaaaggg ttccggaagg agaactgcaa ataggaggc cctgggctcc tggctgggcc 900
agcagctgca cctctcctgt ctgtgctcct cggggcatct cctgatgtc cggggctcac 960
cccccttcca gggctggtc ccgcttctc ggaatttggc ctgggctat gcagaggccg 1020
cctccacacc cctccccag gggcttggg gcagcatagc cccaccctt gcggccttg 1080
ctcaggggtg gccctgccc cccctggcac aaccaaatac cactgatgc ccatcatgcc 1140
ctcagacctt tctgggtct gccgctggg gcctgaagac attcctggag gacactcca 1200
tcagaacctg gcagcccaa aactggggtc agcctcaggg caggagtccc actcctccag 1260
ggctctgctc gtcgggggt gggagatgtt cctggaggag gacactcca tcagaacttg 1320
gcagccttga agttgggtc agcctcgga ggagtccac tctcctggg gtgctgcctg 1380
ccaccaagag ctccccacc tgtaccacca tgtgggactc caggaccat ctgttctccc 1440
cagggacctg ctgacttgaa tgccagccct tgcctcctg tgttgcttg ggccacctg 1500
ggctgcaccc cctgccctt ctctgcccc tccctaccct agccttgctc tcagccacct 1560
tgatagtcac tgggtccct gtgactctg accctgacac cctcccttg gactctgct 1620
gggctggagt ctagggtggt ggctacattt ggcttctgta ctggctgagg acaggggagg 1680
gagtgaagt ggtttgggtt ggcctgtgtt gccactctca gcacccaca tttgcatctg 1740
ctggtggacc tgccaccatc acaataaagt ccccatctga tttttaaaaa aaaaaaaaaa 1800
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa acaaaaaana aaaaaaaatg 1860
ggaataaaaa taacaaaaaa at 1882

```

&lt;210&gt; 302

&lt;211&gt; 2804

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 302

```

gattccaacg catcccagtc cctgtgtgac atcatccgcc tgagccggga gcagatgatc 60
caagtccagg acagcccaga gcctgaccaa ctgctggcca ccctggagaa gcaggagacg 120
attgagcagc tcttaagcaa catgttcgag ggggagcaga gccagtctgt catcgtcagt 180
gggatccagg tgctgctgac mctgctggag cccaggaggc cgaggtccga gtccgtgacc 240
gtgaacagct tcttcagcag tgtggatggg cagctggagc tcctggccca gggggcctgg 300
aaagcactgt gtccagtgtg ggcgccttgc acgccctacg cccgcggtc agctgcttcc 360
accagtcctt gctggagcct cccaagctgg agccgctaca gatgacatgg ggcatgctgg 420
ctcgcctctg ggcaacacgc ggctgcacgt ggtcaagctc ctggccagtg ccctgagcgc 480
caatgatgca gycctgacgc acgagctcct ggcactggac gtgcccacaa ccatgctgga 540
cctcttcttc cattatgtct tcaacaactt cttgcatgcc caagtagagg gatgcgtgag 600
caccatgctg agcttggggc cacytcctga cagcagccct gagacgcca tccaaaaccc 660
tgttggtgaaa catctgctgc agcatgccgc ctgggtggag ggatcctgac gtccctgggag 720
gagaacgacc gtgtacagtg tgcgggaggc cctcggaagg gctacatggg tcacctgaca 780
agagtggccg ktgcctggt gcagaacacg gagaaggggc ccaatgcaga gcagctgagg 840
cagctgctga aggagctgcc cagcgagcag caggagcagt gggaagcctt cgtatcgggg 900

```

```
ccccctggcgg agaccaacaa gaagaacatg gtggacctgg tgaacaccca ccacctacac 960
tcctccagtg acgatgagga cgaccggctc aaggagttca acttccctga ggaggctgtg 1020
ctgcagcagg ccttcagga cttccagatg cagcgcatga cctctgcctt cattgaccac 1080
ttcggcttca atgatgagga gtttggggag caggaggaga gtgtgaacgc accttttgac 1140
aagacagcca acatcacctt ctccctcaat gctgacgatg agaaccccaa cgccaaccta 1200
cttgagatat gctacaagga ccgcatccag cagtttgatg atgatgagga agaggaggac 1260
gaggaagagg cccaggggctc aggggagtct gatggagaag atggcgctg gcagggcagc 1320
cagctggcca ggggggcccg tctgggccag ccacctggtg tccggagtgg aggcagcaca 1380
gacagtgagg acgaagaaga ggaggacgag gaggaggagg aagacgagga gggcattggc 1440
tgtgcagccc gtggaggggc caccctctctg tcctacccca gccctggccc tcagcctcca 1500
ggccccagct ggacagccac ctttgaccca gtgcctacag atgccccgac cagccccga 1560
gtctccgggg aggaagagct gcacactggg cctccagccc cacaggggcc cctcagtgtg 1620
ccccagggcc tccccactca gagcctggcc agcctcctg cccgtgacgc cctgcagctc 1680
aggtctcagg accccacacc cccctcagca cctcaggaag ccacagaagg cagcaaagtc 1740
acggagccct cagccccttg ccaggccttg gttagcatcg gggacctca ggccaccttc 1800
cacgggatcc gttctgcccc cagctcctcg gacagtgcaa ccagagaccc ctctacctct 1860
gtcccagcct ccggggccca ccagccccc cagaccacag aaggggagaa gagcccagag 1920
cccttggggc tccccaaag ccagagtgcc caggccctca cgctcctcc gatacccaat 1980
ggctctgccc cggaagggcc tgcatcccca ggctcccaat agctgcctgg tgcggcasgg 2040
cggccaaatc ttccgtcctc ccgtggatct cccggggtgg gggcagggcg ggtcccacga 2100
tgcccccat tgccctcatc accctgacac cccacattc tctcctctgg acccccagga 2160
ggctggtgcc agggagacag gccaaccca ccccatctt cactgagaag agaagttttg 2220
gagcgttgcc tcctagaata aagatacaga gagtcaaata gagagaatgg agagagagaa 2280
acatatatta tatattatat agagagaggg aggagagcga gagagagtga ggacaccgaa 2340
ctgggctggc ggctccaaag cacagccttc cctgttccgt cccagcggga gctggtgta 2400
ggggtcccaa ggttgccacc cacgtgccc cgtgtcccac gctgcagcgc agacggccac 2460
gcccacaccc ggcttttag ctcaggtcca ccatggggga cggcccagcg tgggtggggg 2520
tgccagaggg tcccgagtgg gggccgtgcc tttgcccaga ccttgcactt tcaaccaggc 2580
cagtcgggct ctggggagca ggggcctccc cggcaacagc cccaggggcc ttgagggctc 2640
gaggtcccag cctgttgcc aagtgaacct gtccccagct cctcctccc aggtggtgt 2700
gagtgtgcgt gcgtttgtgc cgagcttcta ttcatattg caaatataaa taaaggaagg 2760
cagtttacga aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aacc 2804
```

<210> 303

<211> 3859

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (581)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (889)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (890)



<223> n equals a,t,g, or c

<400> 303

```

aagactgcat agggctcgcc gtggggtctc tcaggtgatg gcagaggagc caggcacaac 60
agggaagtaa gaggaagca tatgtggagg catggaagga tggaagaaac agcctggaga 120
tcctgggaaa ctgctaccag ttcagagagg ggtgtggggg gttggtggca ctatgtggcg 180
cgtctgtgcg cgacgggctc agaatgtagc cccatgggag ggactcgagg ctcggtggac 240
ggccttgca gaggtagccg gaactccacg agtgacctcg cgatctggcc cggctcccg 300
tcgtcgcaac agcgtgacta caggggtatg cgggggtccg gcaactgtgc gctggacccc 360
cagttctggg gccacgccc ggaaccgctt actgctgcag cttttggggg cggccggccg 420
ccgctattac agtcttcccc cgcacagaa ggttccattg ccttctcttt cccccacaat 480
gcaggcaggc amcatagccc gttgggaaaa aaaagagggg gacaaaatca atgaagtgga 540
cctaattgca gaggttgaaa ctgataaagc cactgttgga ntttgagagc ctggaagagt 600
gttatatggc aaagatactt gttgctgaag gtaccagga tggtcccatc ggagcgatca 660
tctgtatcac agttggcaag cctgaggata ttgaggcctt taaaaattat acactggatt 720
cctcagcagc acctacccca caagcggccc cagcaccaac ccctgctgcc actgcttcgc 780
cacctacacc ttctgctcag gctcctggta gctcatatcc ccctcacatg caggtacttc 840
ttcctgcctt ctctcccacc atgacctagg gcacagttca gagatgggnn aaaaaagtgg 900
gtgagaagct aagtgaaggr gacttactgg cagagataga aactgacaaa gccactatg 960
gttttgagct aggaagaaa ggttatctgg caaaaatcct ggtccctgaa ggcacaagag 1020
atgtccctct aggaacccca ctctgtatca ttgtagaaaa agaggcagat atatcagcat 1080
ttgctgacta taggccaacc gaagtaacag atttaaaacc acaagygcc aacactaccc 1140
caccocgggt ggccgctgtt cctccaactc cccagccttt agctcctaca ccttcagcac 1200
cctgcccagc tactcctgct ggaccaaagg gaagggtgtt tgtagccct cttgcaaaga 1260
agttggcagt agagaaaggg attgatctta cacaagtaaa agggacagga ccagatggta 1320
gaatcaccaa gaaggatatc gactcttttg tgcctagtaa agttgctcct gctccggcag 1380
ctgttgtgcc tcccacaggt cctggaatgg caccagttcc tacagggtgc ttcacagata 1440
tcccacatcag caacattcgt cgggttattg cacagcgatt aatgcaatca aagcaaacca 1500
tacctcatta ttacctttct atcratgtaa atatgggaga agttttgttg gtacggaaag 1560
aacttaataa gatattagaa gggagaagca aaatttctgt caatgacttc atcataaaag 1620
cttcagcttt ggcatgttta aaagtccccg aagcaaattc ttcttggtat gacacagtta 1680
taagacaaaa tcatgttgtt gatgtcagtg ttgcggtcag tactcctgca ggactcatca 1740
cacctattgt gtttaatgca catataaaag gagtggaac cattgcta at gatgttgttt 1800
ctttagcaac caaagcaaga gagggtaa ac tacagccaca tgaattccag ggtggcactt 1860
ttacgatctc caatttagga atgtttggaa ttaagaattt ctctgctatt attaaccac 1920
ctcaagcatg tattttgga attggtgctt cagaggataa actggtccct gcagataatg 1980
aaaaaggggt tgatgtggct agcatgatgt ctgttacact cagttgtgat caccgggtgg 2040
tggtatggagc agttggagcc cagtggcttg ctgagtttag aaagtacctt gaaaaaccta 2100
tcactatgtt gttgtaacta actcaagaat ttctaaactc tcccagggtca cactgattca 2160
ttcttaacaa gatatttata tgttattaaa caggtgggtc tttttatttt aaccagttat 2220
ttttattatt gagtctgtcc agataagtta ttataatgg gcattactga atttttaaaa 2280
tgccgattac acccaaatat tgtgcacatt taataatcag acaccagatt tttagctctg 2340
tactccta at taaggacat gtatgtggcc ttgcctagcc ctttggtgat aagtacttcc 2400
tctaggaaat gtacgatagg tagaattgtg gttccctaaa gacaagtaca taaagtgac 2460
cctgatgaaa ccttgaagtt ctgaaattta actgcctaaa atgttctcct tagatgtgag 2520
agaaagagaa atcaggaaaa ttaattctct tgggggaagg gcttgaattg aagctttact 2580
ttaagaattta gccctgggtt gaaattttcc attacatgat cttggtttat catcgatggg 2640
aagggtagaa aacttcaagg aaaataagtg aaattttaaa agtcagcatt ttcttagacc 2700
tcttcagctg attgtttatt tttctatgaa ttccctacaca tggttattcc cccctacttg 2760
agataatcta aatataaacc agctacttga tgtaactgar aatttgtgtg gatattttat 2820
taacaaatg tgtaattttg agtacagaat tcaacagtta cctccaaaaa agaaacattg 2880

```

```

ttaatataat ttaacagaag ttgtgaaact aaaattttct aagattaact ggtagttcat 2940
tgtaaatgaa cataatgaac agaatttatg actccactgt ggaaaatgct atcaaataac 3000
taaggaatat atatggaata agtgtacata tgtaaaatat tgttactaga gttagatatg 3060
tgccaaagtc catttatccc aaatcctgtc tgaaaaggag gggtagattg gtaaacattt 3120
tggagtgcct aaaaatgcc aaaaacaaat ggtaatttct actttgataa agtaaaaaag 3180
ttaaatgtgt gtaaaaaagt gttctgtgtc cttctactcc agcatcgtct catgtaaaat 3240
aagaaagccc taaaatacta ttggagagaa aaaattaact aggttgctac tttatttgcc 3300
taaatacttt tttctatttt gttagatttt gcctttcttt tggaaggag gaggcgatat 3360
tctgsattat aaaaatgaat tgggaacatt atcacaattc cagactttct attaatattt 3420
atgtgtttta ataaacgttt gaaattattt atgactactt aaaatgaatc tgaccagtgc 3480
ttccygggat atgtaatatg tggagttagc cctgaaatt tgctttaagt gtttcagtgt 3540
tgaatctgtt tctaaatatt cattattaca tggtagacaa gtgacactcc atatatcca 3600
cacagacttt taccttgctg tattattatg aaaacaatac attaatgtga tttttcagta 3660
attagtaatt ttagggtgaa gattatccaa aagaaacaag cttatcaca gggaccatca 3720
tcaatatgat ccaaactctg ttcaaacatt caaaacttca aagataattc atctttcgct 3780
aatgctgtgt gttctgttgt tcccttgaaa aaaaataaaa acagttgcct tctaataaac 3840
attgttgagt taaaaatta 3859

```

<210> 304

<211> 3378

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (29)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1350)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3361)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3365)

<223> n equals a,t,g, or c

<400> 304

```

tagttctaga tcgcgagcgg ccgacgagnc ggcgctgtgc ctgcagtgcg atatgaacga 60
ctgctatagc cgctgcgga ggctggtgcc caccatcccg cccaacaaga aagtcagcaa 120
agtgagatc ctgcagcacg ttatcgacta catcctggac ctgcagctgg cgctggagac 180
gcacccggcg ctgctgaggc agccaccacc gccgcgccc ccacaccacc cggccgggac 240
ctgtccagcc gcgcgccgc ggaccccgct cactgcgctc aacaccgacc cggccggcgc 300
ggtgaaacaag caggcgagca gcattctgtg ccgctgagcc gcgctgtcca ggtgtgcggt 360
cgctgagcc cgagccagga gcactagaga gggaggggga agagcagaag ttagagaaaa 420

```

aaagccaccg gagaaaggaa aaaacatcgg ccaacctaga aacgttttca ttcgtcattc 480  
caagagagag agaggaaaga aaaatacaac tttcattcct tctttgcacg ttcataaaca 540  
ttctacatac gtattctcct ttgtctcttc atttataact gctgtgaatt gtacatttct 600  
gtgttttttg gaggtgcagt taaactttta agcttaagtg tgacaggact gataaataga 660  
agatcaagag tagatccgac tttagaagcc tactttgtga ccaaggagct caatttttgt 720  
tttgaagctt tactaatcta ccagagcatt gtagatattt tttttttaca tctattgttt 780  
aaaatagatg attataacgg ggcagagaac tttcttttct ctgcaagaat gttacatatt 840  
gtatagataa atgagtgaca tttcatacca tgtatatata gagatgttct ataagtgatga 900  
gaaagtatat gctttaatag atactgtaat tataagatat ttttaattaa atattttttt 960  
gtaaatatta tgtgtgtgtt tttttttaat ctatgggaat atttcttttg gaaaatcatt 1020  
tttcagctca attacagagc tcttgatata ttgaatgtct tttctgtttg gcctggctct 1080  
taatttgctt ttgttttgcc cagtataagc tcggaagtaa cagttatagc tagtggtctt 1140  
gcatgattgc atgagatgtt taatcacaaa ttaaacttgt tctgagtgca ttcaaatgtg 1200  
tttttttaaa tgtagattga aatctttgtt tttgaagcat acatgttgaa artacacctt 1260  
atcagttttt aagtacaggg ttttatagtg taatatatac agagtaagtg tttgtttttg 1320  
tttttcaact gaggtcaaaa tggattctgn aatgattttg catatgggat gaggaatgc 1380  
ttggatcctt aaggagttta cgaaatctgc tgttttatca aagtgaaaaa aaattgtcta 1440  
ttactcttca ttttactacta aagcttaatg tcactaagtt tcatgtctgt acagattatt 1500  
taaatcatgg aaatgaaaaa aatgttctct gcttgctacc aaaggacaaa ctcttgaaa 1560  
tgaacacttt ctgcttttct tcctccaaag aattaatagg caacagtggg agaaaaaaa 1620  
ggcataatgg caaatccttc aagcagggat aaaagtcgat cttcaaacat taacttaagc 1680  
agaccaaaaa ttctgatgac cgcactctaga ttattttttt ataaaaatga ttttactat 1740  
agctatgtta cgctaagcta ctgtccaatc tcttgatgat tgtaactttt acatgtgaat 1800  
attaaagtag atttctctgt cttgtactgt gatttctggg ctcatcttct taaaacctta 1860  
ctcatctttc ttttaaggct cttttttctc cttaaggaag gtaatatttt ctaggttaga 1920  
taggactatc aggggttttg aacattatgc atttaatgtt atgggtactt tacacacaag 1980  
ttagatggaa tttttagagt gaaagaatta agtaggattt aattgggtgc tttgtaata 2040  
gtcaactgtg tgtataacgt ggtctgtttg atttttaaaa ggaaaggatt tgtttcagat 2100  
tatacaagaa taaaagtatt atagacccaa gggacttctt atgaggtaa attcagatat 2160  
ttatatgaat atgaaatacc atggtcccta gtatgcagtt gaagtggcaa tgtctaaaca 2220  
gaaatgaaca aaactaatgc tagcagggtt aaatcaatca aaatgtttaa aaattgattc 2280  
tgtcctcagc atgttayttc ctcagctctg ataatttact ggtcttgagt attttgagaa 2340  
tttgatgttg aacgttataa agtcaaagaa ctgcttggtt agatgaggtt tatttttatt 2400  
tttgatatta ttcatctttg tcacacatca agaagaaaac actagagtgc tgctggaatt 2460  
ccaaatctga agaattctaa cgactgcatt ctttggtatt aaaaagggca caatccttcc 2520  
tttttatttg gcagtttaat ttcagtagga agcatgtcac atgtgcactg ttggttagaa 2580  
ttatgcatct gtcatgcctg actgtgaac cctacctaag ccttttggtg cagtttaaaa 2640  
cttatactgg tggactgtga acctcaaaac aaatgggtat ttttggtttt tgaggataga 2700  
tgttactcct taaagtgtt atttggggca tgaaaaacta ctgaaagaag aaaagtgc 2760  
cagatactac atttcaaaga gttggcattt tccctttggc cactcaagca gcatttgatg 2820  
tatctaaaga aacaaagtca ttgtttattt tttaaaaaat tatatgcagt tgtacaagat 2880  
actacattcc attgaaatgt tggctatgtc ctaaccaggc aaccagataa caaaaacatt 2940  
ttgagtcctt tatctaggta gttctaatta ttcagctact tagtttaaca aaggaaaata 3000  
tcctgacttc tctcatttca tttgtagact tttcattgta taggcacaac caaagagtca 3060  
gactgggtta aaactccaga aggaaaaaaa gtatcccaca cagtggatgt tgtttctaag 3120  
aatgctacaa aatcctgaca tctcagacat ctcaatgtta aaggaaagaaa aaaaatacct 3180  
tttcatttca aagaactaat atactttgat attgtgtaaa ccttactcaa gtttattgtc 3240  
aagctttaac tgccttttta gaacttttta aaatttcgag cccacaaatc tattgtatta 3300  
gttgcttct ataacaataa atcttcaact agcaaaaaaa aaaaaaaaaa aaaaaaaaaa 3360  
nccnggggg gggggccc 3378

<210> 305  
<211> 1014  
<212> DNA  
<213> Homo sapiens

<400> 305  
cagcggcggc ggcggcgcca ggatgatcaa gctgttctcg ctgaagcagc agaagaagga 60  
ggaggagtgc ggcggcgcca ccaagggcag cagcaagaag gcgtcggcgc cgcagctgcg 120  
gatccagaag gacataaacg agctgaacct gcccaagacg tgtgatatca gcttctcaga 180  
tccagacgac ctctcaact tcaagctggt catctgtcct gatgaggcct tctacaagag 240  
tggaagtgtt gtgttcagtt ttaaggtggg ccagggttac ccgcatgac cccccaaggt 300  
gaagtgtgag acaatggtct atcaccccaa cattgacctc gagggcaacg tctgcctcaa 360  
catcctcaga gaggactgga agccagtcct tacgataaac tccataatth atggcctgca 420  
gtatctcttc ttggagccca acccgagga cccactgaac aaggaggccg cagaggctct 480  
gcagaacaac cggcggtgtt ttgagcagaa cgtgcagcgc tccatgcggg gtggctacat 540  
cggctccacc tactttgagc gctgcctgaa atagggttg gcgataccca ccccgccac 600  
ggccacaagc cctggcatcc cctgcaaata tttattgggg gccatgggta ggggtttggg 660  
ggcgggcccg tgggggaatc ccctgccttg gccttgctc cccttcctgc cacgtgcccc 720  
tagttatttt tttttttta acaccatgtg attaaggtcg gcgctgcctc ccccgaccca 780  
ctcagcgatg ggaaatgaat tggcttgtct agccccctg ctgggtgctt gttcagcccc 840  
cactctgggc tgtggagtgg gtgggcaacg ggctgggta gctgggcca ggcaaccac 900  
ccctccacct ctggaggtcc caccaggcta ttaaagggga atgttactgc aaaaaaaaaa 960  
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 1014

<210> 306  
<211> 2127  
<212> DNA  
<213> Homo sapiens

<400> 306  
ggaggaggcg ccgagctgac cggcgacgc cgcgggaggt tctggaaacg ccsggagctg 60  
cgagtgtcca gacacttccc tctgtgacca tgaaactctg ggtgtctgca ttgctgatgg 120  
cctggttttg tgtctgagc tgtgtgcagg ccgaattctt cacctctatt gggcacatga 180  
ctgacctgat ttatgcagag aaagagctgg tgcagtctct gaaagagtac atccttgtgg 240  
aggaagccaa gctttccaag attaagagct gggccaacaa aatggaagcc ttgactagca 300  
agtcagctgc tgatgctgag ggctacctgg ctccacctgt gaatgcctac aaactggtga 360  
agcggctaaa cacagactgg cctgcgctgg aggacctgt cctgcaggac tcagctgcag 420  
gttttatcgc caacctctct gtgcagcggc agttcttccc cactgatgag gacgagatag 480  
gagctgccaa agccctgatg agacttcagg acacatacag gctggaccca ggcacaatth 540  
ccagagggga acttcagga accaagtacc aggcaatgct gagtgtggat gactgctttg 600  
ggatgggccc ctcggcctac aatgaagggg actattatca tacgggtgtt tggtggagc 660  
aggtgctaaa gcagcttgat gccggggagg aggccaccac aaccaagtca caggtgctgg 720  
actacctcag ctatgctgtc ttscagtttg gtgatctgca ccgtgccctg gagctcacc 780  
gccgcctgct ctcccttgac ccaagccacg aacgagctgg agggaatctg cgtactttg 840  
agcagttatt ggaggaagag agagaaaaaa cgtaacaaa tcagacagaa gctgagctag 900  
caaccccaga aggcattctat gagaggcctg tggactacct gcctgagagg gatgtttacg 960  
agagcctctg tcgtggggag ggtgtcaaac tgacacccc tagacagaag aggcctttct 1020  
gtaggtacca ccatggcaac agggccccc acgtgctcat tgccccctc aaagaggagg 1080  
acgagtggga cagcccgcac atcgtcaggt actacgatgt catgtctgat gaggaaatcg 1140  
agaggatcaa ggagatcgca aaacctaaac ttgcacgagc caccgttctg gatcccaaga 1200  
caggagtcct cactgtcgcc agctaccggg tttccaaaag ctctggcta saggaagatg 1260

```

atgaccctgt tgtggccga gtaaactcgtc ggatgcagca tatcacagg ttaacagtar 1320
agactgcaka attgttacag gttgcaaatt atggagtggg aggacagtat gaaccgcact 1380
tcgacttctc taggaatgat gagcgagata ctttcaagca tttagggacg gggaatcgtg 1440
tggctacttt cttaaaactac atgagtgatg tagaagctgg tgggtgccacc gtcttccctg 1500
atctgggggc tgcaatttgg cctaagaagg gtacagctgt gttctggtac aacctcttgc 1560
ggagcgggcg aagggtgacta ccgaacaaga catgctgcct gccctgtgct tgtgggctgc 1620
aagtgggtct ccaataaagt gttccatgaa cgaggacagg agttcttgag accttggtga 1680
tcaacagaag ttgactgaca tccttttctg tccttccctc tcctggctct tcagcccatg 1740
tcaacgtgac agacaccttt gtatgttcct ttgtatgttc ctatcaggct gatttttggg 1800
gaaatgaatg tttgtctgga gcagagggag accatactag ggcgactcct gtgtgactga 1860
agtcccagcc cttccattca gcctgtgcca tccctggccc caaggctagg atcaaagtgg 1920
ctgcagcaga gttagctgtc tagcgcctag caagggtcct ttgtacctca ggtgttttag 1980
gtgtgagatg tttcagtga ccaaagttct gataccttgt ttacatgttt gtttttatgg 2040
catttctatc tattgtggct ttacaaaaaa ataaatgtc cctaccagaa gccttaaaaa 2100
aaaaaaaaaa aaaaaaaaaa ggcggcc 2127

```

&lt;210&gt; 307

&lt;211&gt; 666

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (588)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (664)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 307

```

gtgccctgac tgcctgacgg ccgcgcaggg ccttgcagga ccgctgggga ggatgttgtt 60
aacgtaaaga gccaggctga tgaggaaggt tcatgagtc tttgggtata agcgggagtt 120
ggggcgggcg gaaggcagat gactctgaga agggcaagca ctttaacctt ttaagcccaa 180
ccagatgagt tgcctgcagt tttggaggcc ttcagagcat ttcactagac ctctgtctgt 240
gtcgggtccag tgtcttttagc caagctttga ttaaagatga cttccttgtt tgctcaagaa 300
attcgccttt ctaaaagaca tgaagaaata gtatcacaaa gattaatgtt acttcaacaa 360
atggagaata aattgggtga tcaacacaca gaaaaggcat ctcaactcca aactgttgag 420
actgctttta aaaggaacct tagtctttta aaggatatag aagcagcaga aaagtcacta 480
cagaccagga ttcacccact tccacggcct gaggtggttt ctcttgagac tcgttactgg 540
gcatcataga agaatatatt ccaaagtggg aacagtttct tttagggnga gcaccatatt 600
cttttgcctg tgaaaatcaa aatgaagcag aaaataccat tcaaatagag gcacagcgat 660
aacntc 666

```

&lt;210&gt; 308

&lt;211&gt; 2171

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

<221> misc feature  
<222> (1248)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2162)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2166)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (2168)  
<223> n equals a,t,g, or c

<400> 308  
cctcggcggt acccgagct tcaggcccca ccggggcgcg gagagtccca ggcccggccg 60  
ggaccgggac ggcgtccgag tgccaatggc tagctctagg tgtcccgtc cccgcgggtg 120  
ccgctgcctc cccggagctt ctctcgcatg gctggggaca gtactgctac ttctcgccga 180  
ctgggtgctg ctccggaccg cgctgccccg catattctcc ctgctggtgc ccaccgcgt 240  
gccactgctc cgggtctggg cggtgggcct gagccgctgg gccgtgctct ggctgggggc 300  
ctgcggggtc ctacaggcaa cggttggctc caagagcgaa aacgcagggtg cccagggtg 360  
gctggctgct ttgaagccat tagctgcggc actgggcttg gcctgccggg acttgccctg 420  
tyccgagagc tgatctcatg gggagccccc gggtccgcgg atagcamcag gctactgcac 480  
tggggaagtc accctaccgc cttcgttgte agttatgcag cggcactgcc cgcagcagcc 540  
ctgtggcaca aactcgggag cctctgggtg cccggcggtc agggcggtc tggaaacct 600  
gtgcgtcggc ttctaggctg cctgggctcg gagacgcgcc gcctctcgct gttcctggte 660  
ctgggtgtcc tctcctctct tggggagatg gccattccat tctttacggg ccgcctcact 720  
gactggattc tacaagatgg ctacgccgat accttactc gaaacttaac tctcatgtcc 780  
attctacca tagccagtgc agtgcaggag ttctgggtg acgggatcta taacaacacc 840  
atgggccacg tgcacagcca cttgcaggga gaggtgtttg gggctgtcct gcgccaggag 900  
acggagtgtt tccaacagaa ccagacaggt aacatcatgt ctcggttaac agaggacacg 960  
tccaccctga gtgattctct gagtgagaat ctgagcttat ttctgtggtg cctggtgcga 1020  
ggcctatgtc tcttgggat catgctctgg ggatcagtgt ccctcaccat ggtcacctg 1080  
atcacctgc ctctgctttt cttctgccc aagaaggtgg gaaaatggta ccagttgctg 1140  
gaagtgcagg tgcgggaatc tctggcaaag tccagccagg tggccattga ggctctgtcg 1200  
gccatgccta cagttcgaag ctttgccaac gaggagggcg aagccagnaa gtttagggaa 1260  
aagctgcaag aaataaagac actcaaccag aaggaggctg tggcctatgc agtcaactcc 1320  
tggaccacta gtatttcagg tatgctgctg aaagtgggaa tcctctacat tggtagggag 1380  
ctggtgacca gtggggctgt aagcagtggg aaccttgta catttgttct ctaccagatg 1440  
cagttcaccc aggtgtgga ggtactgtc tccatctacc ccagagtaca gaaggctgtg 1500  
ggctcctcag agaaaatatt tgagtacctg gaccgcacc ctcgctgccc acccagtggt 1560  
ctgttgactc cttacactt ggagggcctt gtccagtcc aagatgtctc ctttgectac 1620  
ccaaaccgcc cagatgtctt agtgctacag gggctgacat tcaccctacg ccctggcgag 1680  
gtgacggcgc tggggggacc caatgggtct gggaaagagca cagtggctgc cctgctcgag 1740  
aatctgtacc agcccaccgg gggacagctg ctggtggatg ggaagccct tcccaatat 1800  
gagcaccgct acctgcacag gcagggtggct gcagtgggac aagagccaca ggtatttga 1860

241

```
agaagtcttc aagaaaatat tgcctatggc ctgacccaga agccaactat ggaggaaatc 1920
acagctgctg cagtaaagtc tggggcccat agtttcatct ctggactccc tcagggttat 1980
gacacagagg tagacgaggc tgggagccag ctgtcagggg gtcagcgaca ggagtggtcg 2040
ttggcccgag cattgatccg gaaaccgtgt gtacttatcc tggatgatgc caccagtgcc 2100
ctggatgcaa acagccagtt acaggtggag cagctcctgt acgaaagccc tgagcggtag 2160
tnccgntnaa g 2171
```

&lt;210&gt; 309

&lt;211&gt; 6163

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (6132)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (6135)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (6158)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 309

```
aattcggcac gagcacagcc tgagcatact ctgtgcatta ggaagacctg agtgcatttc 60
ccaccattgt cctttccaca ttatgttgta gctggctggc tgtmaggcga ctacaagact 120
gaggggtsttg tgccttatag atstttgtat ccccatggc tgacacatag taggtactca 180
gtaaatggtt ttataatgaa tcagtgaaca ttttgcttct atagaagtgt accttctttg 240
ttcttatatt atgaaacctc tttattagaa tttgtgattg attctgacag tgtatagatt 300
taccttatat tgtctttatt ttccatgagc tactaagtca ttagagatac tctgaagcat 360
agttagttta ggaaatcact tcatattgat tgtattagaa ttatcttggg attgaagata 420
tatccctaga gcaggggacc ccaaccccca ggccatgggc cacacagcag gaagagggtga 480
gtgggtgggc attgaggagc ttcatctgta tttatggcta cttcccatca ctggaattac 540
cacctgaact ccacctcttg tcagctcagt ggcagcatta gattctcata gragcacaaa 600
tcctattgtg aactctgcat gcaagggatc taggctatgc gctccttatg agaactctaa 660
gcctgatgac ctgaggtgka acagtttcat cctgaaacca cccttcaccc tgcagtctgt 720
ggaaaaattg tcttccacaa aactgggtccc tggtgccaaa aatgktgggg accgctgctc 780
tagagagagg tcatgatatc ataccaacca aatggaaatr acaaatgttt tatgtcaagt 840
gttaattgca gaaataaatc tttttttttt ttttttggtg gaaaacaaag aggcatactc 900
tgatttttat actctgtttt tgcaggtgct cttttctttg aatggagatt tgatgagcaa 960
gtgggttagga tgcagggaga gctactatgg gtgatatttt ccttgtttag gagctgtgag 1020
ttaaattgtg atcctttctg gtttatctaa ggaaagtcaa atcttgacag aaaacatttt 1080
tccttggaag gtcaactctc agacattgta ttttggtttc cctcagtcct cataacttcc 1140
ttcttgctga acatatttta ttctcttttc agagaaggaa aataaaaaagg attctaaaaa 1200
tttgatgcat tggaaaaatt tccttgaggc atttagcaac acatagaaaa tgggcttttg 1260
ttcttttcca aaacttttag ccatagggtc ttttatagac agggatagta aaatgaaaat 1320
tgagaaatat aagatgaaaa ggaatgrtaa aaatatcttt taggggggctt ttaattggtg 1380
```

```

atctgaaatc ttgggagaag ctgttctttt caggcctgag gtgctcttga ctgtcgccctg 1440
cgactgtgtg accccgagca acattctaag ggtgtgcttt cgccttggtt aactcctttg 1500
acctcattct tcatatagta gtctaggaaa aagttgcagg taatttaaac tgtctagtgg 1560
tacatagtaa ctraatttct attcctatga gaaatgagaa ttatttattt gccatcaaca 1620
cattttatac ttgtcatctc caaatttatt gcgcgagac ttgtccattg tgaaaagttag 1680
agaacattat gtttgtatca tttctttcat aaaacctcaa gagcattttt aagccctttt 1740
catcagaccc agtgaaaact aaggatagat gtttaaaaaac tggaggtctc ctgataagga 1800
gaacacaatc caccattgtc atttaagtaa taagacagga aattgacctt gacgctttct 1860
tgtaaataag atttaacagg aacatctgca catctttttt ccttgtgcac tatttgttta 1920
attgcagtgg attaatacag caagagtgcc acattataac taggcaatta tccattcttc 1980
aagacttagt tattgtcaca ctaattgatc gtttaaggca taagatggtc tagcattagg 2040
aacatgtgaa gctaactctg tcaaaaagat caacaaatta atattgttgc tgatatttgc 2100
ataattggct gcaatttatt aatgtttaat tgggttgatc aaatgagatt cagcaattca 2160
caagtgcatt aatataaaca gaactggtag cacttaaaat gataatgatt aacttatatt 2220
gcatgttctc ttctttcac tttttcagt gtctacattt cagaccgagt ttgtcagctt 2280
tttgaaaaac acatcagtag aaaccaagat tttaaaatga agtgcaaga cgaaggcaaa 2340
acctgagcag ttctaaaaa gatttgctgt tagaaatttt ctttgtggca gtcattttatt 2400
aaggattcaa ctggtgatac accaaaagaa gagttgactt cagagatgtg ttccatgctc 2460
tctagcacag gaatgaataa atttataaca cctgcttttag cctttgtttt caaaagcaca 2520
aaggaaaagt gaaagggaaa gagaaacaag tgactgagaa gtcttgtaa ggaatcaggt 2580
tttttctacc tggtaaacat tctctattct tttctcaaaa gattgttgta agaaaaaatg 2640
taagacaaaa aaaaaaaaaa aaaacagagg cagaggcagg cagtagcaag aaagcagagc 2700
gtaacatcag ctagatggta acatgcaatg tcagctctct tgaagacatg ggaaacctaa 2760
gttacacctt ggggttaaaat tcttcaccgt attagttttg ttgcttcata aaattttacct 2820
aagcaagtgg tcttgcttgc ctcaaatcca agcagtcttg aacacttgga ggcaattaat 2880
gagtatatct tagtcaaaag aattgttggg gcttttttatt aaagctgcag tttcagttct 2940
gcttttgggg aattgtgcta tgaaagcagc tgccaaaata agctcattta tttcttcaa 3000
tcccactcag tgctcagtca ctatattctg tttccttttt ttttttcaa gttgcatatt 3060
tggtttcccc ttatgattgg gaaagatgaa ttttcagcag aaaacagtgt ttgttcactt 3120
tcaaagagct atagtttcta aaacatttag agcaataaat attcatcaga ggtaccaagt 3180
aagccagcag aagagttaag ggtagagaa atcccttatt tcatgtcttg actctaaaa 3240
gatcaaaagta cttttccttg taatgtggat ttcttcttat gcggatatgc aaaaacttca 3300
gttatacgta gtaatgctag caggtaattt tagtggacat tttataacaa ctgtcacttt 3360
gttttgccac atgtagagtt tgctcagcta tttccagat atctcccccac aaaaggaggc 3420
aaaggggtacc agcttttcaa tgagcattac ctattacttg gcaaagatga tgaagactct 3480
attaatagtt catttgataa atgttgacat aaccaacaat agagattagg aagttagttt 3540
taagaaatca atagcatata gacattaccc tcatggagt tgtattctac tacttgaact 3600
gattgtagct ataaaagcat agttagatag ctgaatagtt agatcataag caaagaaggc 3660
cagaacacat ctcttatcaa gaaatcaatg aatagttttat ctcattttta aagcaacttt 3720
atccttcttt aattccttcc tttcttctag tgcaaaaacta ctttaataagg ttggtgttta 3780
ggttagtggt cacaccattc ctcatctggt gtgaattacc ttctctttct ttactattta 3840
ctaccaacct agtacatgtg ttgactgaat tcttttcaaa caatgttgag ttatcatggt 3900
gcaccttaata aattaacacc acagattaca gcatccttgc tgattttctc agcaaagcca 3960
gattagatgg aaataaacia agaaaatgat cctagagtga atttttctag aaaatatcta 4020
ttatgaacca tgctgtttta agtattagct tgaaggtgat ggatccagct attcagaaaa 4080
taactttcat ataaccatga ttttgcacag tatgaggtct taaatgtgtg gaaagagata 4140
aattttttat cattaccaca aacctttttt aaagattcaa aggtggaaga aagtgattta 4200
tttttttctc tcagcatata tatataaaag acttgtcaga tgtttaattt ggggaggttg 4260
ataatgaaac atatcaacag agtatagtag ttatagtagt gtttgtgggt aaataatttc 4320
ctgggggtcag acatatataa acatatttgc ttcaaaatga taaaggcatg aaatcagtct 4380
taaaaattga aatgggggtg atgggggaga aaaagaagaa caaatttgaa gtgccctttc 4440

```



```

aaatctgctg gatacaagta ttgaagtttt aagtcacett attctgtctg aaagtgtatt 4500
tttcattcta caatagaccc aatcaacaag acgtataact tgagttgcat gatgttcagt 4560
ttatgtaatc tactgttggg atggttaagaa ttgatgtagg ctgtggtgta agaatagaatt 4620
aaaatatagt ttcactggct tttctctaca tatccactat cacaatggct aggtttcctg 4680
ttgctcactg ttggattctg gagaaaaatt taatgaaaga tgatatcaga ggaagaataa 4740
gtggaggtag agaagaaagg agtgatagag gaggggaaaa aaacaaaaca tttttttgtg 4800
ttatccaaag gagctttttc cttattctgt caagcattga gatcttcttc agctttcaat 4860
gtagttgcta aatacaata atgctactag gtagtgacta aatatagcaa acacttcac 4920
agatattaga attaggtcac actattgagg ttataatctg aaggttggtg tacatagaaa 4980
ccactttaga ttattatcaa cttggactag gctttatttt ataatagcat agtaagtaat 5040
atctattgtg tcatttcttc aaccatttta ttctaagatc catgaagctt cttgaggcca 5100
aataaaataa taagtttaga caagaagtag attgtgactt tttttccctt agagatacta 5160
tttactatct cctatcctga taggtggaag gtttactgaa ttggaaattg gttgactatt 5220
agtttttaac taaaatgtgc aataacacat tgcagtttcc tcaaaactagt ttcctatgat 5280
cattaaactc attctcaggg ttaagaaagg aatgtaaatt tctgcctcaa tttgtacttc 5340
atcaataagt ttttgaagag tgcagatttt tagtcaggtc ttaaaaaata actcacaat 5400
ctggatgcat ttctaaattc tgcaaatgtt tcctggggtg acttaacaag gaataatccc 5460
acaatatacc tagctaccta atacatggag ctgggggtca acccactgtt tttaaggatt 5520
tgcgcttact tgtggctgag gaaaaataag tagttcgagg aagtagtttt taaatgtgag 5580
cttatagata gaaacagaat atcaacttaa ttatgaaatt gtagaacct gttctcttgt 5640
atctgaatct gattgcaatt actattgtac tgatagactc cagccattgc aagtctcaga 5700
tatcttagct gtgtagtgat tcttgaaatt ctttttaaga aaaattgagt agaaagaaat 5760
aaaccctttg taaatgaggc ttggcttttg tgaaagatca tccgcaggct atgttaaaag 5820
gatttttagct cactaaaagt gtaataatgg aaatgtggaa aatatacgtg gtaaaggaaa 5880
ctacctcatg ctctgaagggt tttgtagaag cacaattaaa catctaaaat ggctttgtta 5940
caccagagcc atctggtgtg aagaactcta ttttgtatg ttgagagggc atggaataat 6000
tgtattttgc tggaataga cacattcttt attatttgca gattcctcat caaatctgta 6060
attatgcaca gtttctgtta tcaataaaac aaaagaatcc tgaaaaaaaa aaaaaaaaaa 6120
aaggggggcg cncnaagat cccccaaggg gcccaacnta ccc 6163

```

&lt;210&gt; 310

&lt;211&gt; 2086

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1763)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1769)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 310

```

tcccggtgca agccacgcgt ccgcggmacg wgggtgcgga cgcccggtc ccggcgtgga 60
cgccatggtg ctgtgccgg tgattgggaa gctgctgcac aagcgcgtgg tgctggccag 120
cgctcccca cgcgctcaga gatcctcagc aacgcgggtc tcaggtttga ggtggtcccc 180
tccaagttta aagagaagct ggacaaagcc tccttcgcta ctccgtatgg gtacgccatg 240
gagaccgcca agcagaaggc cctggagggt gcccaaccggc tgtaccagaa agacctgcgg 300

```

gccccgcagc tggtcattgg agcggacacg atcgtgacag tcggggggct gattctggag 360  
aagccggtgg acaagcagga cgcctacagg atgctgtccc ggttgagtgg gagagaacac 420  
agcgtgttca cagggtgtcg gatcgccac tgctccagca aagaccatca gctggacacc 480  
agggtctcgg aattctacga ggaaacgaag gtgaagttct cggagctgtc cgaggagctg 540  
ctctgggaat acgtccacag cggggagccc atggacaaag ctggcggcta cgggatccag 600  
gccctgggcg gcatgctggt ggagtcctga caccgggact ttctgaacgt ggtgggattc 660  
ccgctgaacc acttctgcaa gcagctggtg aagctctact acccgccccg yccggaggac 720  
ctgcggcgga gtgtcaagca cgactccatc ccggccgcgg acaccttcga agacctcagt 780  
gacgtggagg ggggcggctc ggagccact cagagggacg cgggcagccg cgatgagaag 840  
gccgaggcgg gagaggcggg acaggccacg gcagaggctg agtgtcacag gactcgggag 900  
accctgcctc cgttccccgac acgcctcctg gagctgattg agggctttat gctatccaa 960  
ggcctgctca ccgcttgcaa actgaagggtg ttcgatttgt taaaagatga agcaccaccag 1020  
aaggctgcgg atattgccag caaagtggac gcctctgcgt gtggaatgga gaggcttctg 1080  
gacatctgtg ctgccatggg gctcctggag aagacagagc aaggttacag taacacagag 1140  
acagcgaacg tctacctggc atcggatggc gaatactctc tgcacggctt catcatgcac 1200  
aataatgacc tcacatggaa cctctttaca tacctggagt ttgccatccg agagggaaca 1260  
aaccagcacc acagggcgtt ggggaagaag gcggaagatc tgttccagga tgcgtactac 1320  
cagagcccgg agacgcggct gaggttcatg cgggccatgc acggcatgac gaagctgact 1380  
gcgtgccagg tggccacggc cttcaatctg tcccgttct cctccgctg cgactggga 1440  
ggctgcaccg gtgcaactggc ccgagagctg gcccgtagt accctcgtat gcaggtgact 1500  
gtgtttgacc tcccagacat tatcgagctg gccgcccact tccaaccccc cggaccgcag 1560  
cagtgcatgat ccacttcgca gcaggtgact ttttcaggga cccctcccc agcgtgagc 1620  
tgtacgtcct gtgccggatc ctgcatgayt ggccagacga caaagtccac aagttactca 1680  
gcagggctcg cgagagctgc aagccagggg ccggcctgct gctgggtggag acgctcctgg 1740  
atgaggagaa gaggggtggc cangcgcct gatgcagtca ctgaacatgc tgggtgcagac 1800  
tgaaaggcaag gagcggagcc tgggcgagta tcagtgcctt ctggagctgc acggcttcca 1860  
ccaggtgcag gtgggtgcaact tgggggggtgt cctggatgcc atcttgcca ccaaagtggc 1920  
cccctgaagc ccaggcagca tgttcattat agggatgtcc tccccaggc tgcaggtgga 1980  
ccgcccggtc cccaagtacc ataggacagt cacataggag cgtgtagtcg tgactgaata 2040  
aagaaagcaa aagccaaaaa aaaaaaaaaa aaaaatttgg gggggg 2086

&lt;210&gt; 311

&lt;211&gt; 2163

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 311

gcggccgcag ctccctcacc agcttggtgg tgggcgtgtt cgtgggtctac gtgggtgcaca 60  
cctgctgggt catgtacggc atcgtctaca cccgcccgtg ctccggcgac gccaaactgca 120  
tccagcccta cctggcgcgg cggcccaagc tgcagctgag cgtgtacacc acgacgaggt 180  
cccacctggg tgctgagaac aacatcgacc tggctctgaa tgtggaagac tttgatgtgg 240  
agtccaaatt tgaaaggaca gttaattgtt ctgtacaaa gaaaacgaga aacaatggga 300  
cgctgtatgc ctacatcttc ctccatcacg ctggggctct gccgtggcac gacgggaagc 360  
aggtgcacct ggtcagtcct ctgaccacct acatggctcc caagccagaa gaaatcaacc 420  
tgctcaccgg ggagtcctgat acacagcaga tcgaggcgga gaagaagccg acgagtgccc 480  
tggtatgagc agtgctccac tggcgaccgc ggctggcgct gaacgtgatg gcggacaact 540  
ttgtctttga cgggtcctcc ctgcctgccg atgtgcatcg gtacatgaag atgatccagc 600  
tggggaaaac cgtgcattac ctgcccaccc tgttcacga ccagctcagc aaccgcgtga 660  
aggacctgat ggtcataaac cgctccacca ccgagctgcc cctcaccgtg tcctacgaca 720  
aggtctcact ggggcggctg cgcttctgga tccacatgca ggacgccgtg tactccctgc 780  
agcagttcgg gttttcagag aaagatgctg atgaggtgaa aggaattttt gtagatacca 840

```
acttatactt cctggcgctg accttctttg tcgcagcggt ccatcttctc tttgatttcc 900
tggcctttta aaatgacatc agtttctgga agaagaagaa gagcatgac gccatgtcca 960
ccaaggcagt gctctggcgc tgcttcagca ccgtggcatc ctttctgttc ctgctggacg 1020
agcagacgag cctgctggtg ctggtcccgc cgggtgttgg agccgccatt gagctgtgga 1080
aagtgaagaa ggcatgaag atgactatct tttggagagg cctgatgcc gaatttcagt 1140
ttggcactta cagcgaatct gagaggaaaa ccgaggagta cgatactcag gccatgaagt 1200
acttgctata cctgctgtac cctctctgtg tcgggggtgc tgtctattca ctctgaata 1260
tcaaataata gagctggtac tcctggttaa tcaacagctt cgtcaacggg gtctatgcct 1320
ttggtttcct cttcatgctg ccccagctct ttgtgaacta caagttgaag tcagtggcac 1380
atctgccctg gaaggccttc acctacaagg ctttcaacac cttcattgat gacgtctttg 1440
ccttcacatc caccatgccc acgtctcacc ggctggcctg cttccgggac gacgtggtgt 1500
ttctggtcta cctgtaccag cgggtggctt atcctgtgga taaacgcaga gtgaacgagt 1560
ttggggagtc ctacgaggag aaggccacgc gggcgcccca caggactga aggccgcccg 1620
ggctgccgcc agccaagtgc aacttgaatt gtcaatgagt atttttgaa gcatttgagg 1680
gaattcctag acattgcgtt ttctgtgttg ccaaaatccc ttcggacatt tctcagacat 1740
ctccaagtt cccatcacgt cagatttgga gctggtagcg cttacgatgc cccacgtgt 1800
gaacatctgt cttggtcaca gagctgggtg ctgccggtca ccttgagctg tgggtggtcc 1860
cggcacacga gtgtccgggg ttccggccatg tcctcacgcg ggcaggggtg ggagccctca 1920
caggcaaggg ggctgttgga tttccatttc aggtggtttt ctaagtgtc cttatgtgaa 1980
tttcaaacac gtatggaatt cattccgcac ggactctggg atcaaaggct ctttctctt 2040
ttgtttgaga gttggtgtt ttaaagctta atgtatgttt ctattttaaa ataaattttt 2100
ctggtgtgtg caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2160
aaa 2163
```

<210> 312

<211> 1397

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1397)

<223> n equals a,t,g, or c

<400> 312

```
ctagctggga ggctgacggc ccgcgggcgt aacrgaactg cagccgcgag ctcttgagg 60
cggcgggatg gagcgggcgg ccgagcctgg aaacctggcc ggcgtcaggc acatcatcct 120
ggtcctctca ggaaaggggg gcgttgggaa aagcaccatc tccacggagc tggccctggc 180
actgcgccat gcaggcaaga aggtgggaat cctggatgtg gacctgtgtg gccccagtat 240
accccgcatg ctccggggcgc agggcagggc tgtgcaccag tgcgaccgcg gctgggcacc 300
cgtcttctct gaccgggagc agagcatctc gctcatgtct gtgggcttcc tgctggagaa 360
gccggacgag gccgtggtgt ggagaggccc caagaaaaac gcgctgataa agcagtttgt 420
gtccgacgtg gcctgggggg agctggacta cctggtggtg gacacgcccc cggggacctc 480
cgatgagcac atggccacca tagaagccct cgtccctac cagccctgg gggccctcgt 540
ggtcaccacg cccagggcgg tgtccgtggg ggacgtgagg cgcgagctga ctttctgtag 600
gaagacgggc ttgcgggtga tgggaatcgt ggagaatatg agcggcttca cctgcccaca 660
ctgcacggag tgcaccagcg tcttctccag gggcggcgga gaggagctgg cccagctcgc 720
cggggtgccc ttcttaggct ccgtgcccct ggaccctgcg ctcatgagga ccctggagga 780
gggccacgac ttcacccagg agttccccgg gagccccgcc ttcgctgcac tcacctccat 840
agcccagaag attctggacg cgacgccgcg gtgcctcccc tgactaaggc caccttgacg 900
ccgctttcca gggccaccaa gggctctgct ccagcctctc agagaaacag aggcctgggc 960
```

246

```
tcggttcccg ggcctgcag gggcaggccc aggcagcgtc agcgggagag cttctcccg 1020
accagcccag cccaggatg tgtcgacca gcagctctgc ctggttggcc tgcagtgccg 1080
tggtctgcgt gctctgcagc tgtgagacgg gggcggcctg ggctctcttc ccatccatgt 1140
tgcctacctg tgcccctggc agccgcgtgt ccacacagtt agcggagcgc aggacttctg 1200
cagtcctcag gtgaccccg gcctccagca ccctgggtcg ctgtcatctg tgtttagctc 1260
ggggagtgcy ccctaagggg gcgaactgac ctcaggcatg tcttgtaact gtagaggcgc 1320
ctgccattaa acgtgtccgc tgctgtggcg acagaaaaaa aaaaaaaaaa aaaaaaaaaa 1380
aaaaaaaaaa aaaaaan                                     1397
```

&lt;210&gt; 313

&lt;211&gt; 4106

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (344)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 313

```
ttactatcag acagccccc aagcagatta cagccaaggt gcaactcagt atactcaagc 60
ccagcaaaact cgacaagtga cagccataaa accagccaca ccaagtccag ctaccactac 120
tttctccatc tatcctgtat cctccaccgt acagccagta gcagctgcgg ctactgtggt 180
gccatcctat actcagagtg ctacttacag taccacagca gttacatatt ctggtacgtc 240
ttattcaggt tatgaagcag cagtgtattc agctgcattc tcctactatc aacagcagca 300
gcagcaacag aagcaggcag cagcagcagc tgtgtgctgt cganactagc tgccctggaca 360
gggaccacct ttactaaaa agcaccattc caaaataaac aactgaaacc aaaacagcct 420
cccaaaccac cacagattca ctattgtgat gtttgtraga tcagctgtgt ggaccacaga 480
cttataaaga acatttagaa ggacagaaac ataaaaaaaa agaagctgca ttgaaagcct 540
cacaaaatac cagcagcagc aacagttcta ctggtgggac tcaaatcag ctacgttgtg 600
agctctgcga tgtgtcttgt acaggagcag atgcgtatgc tgcccacatt cgtggtgcta 660
agcatcagaa agtggttaag ttacacacaa aacttggtta acccattcca tcaacagaac 720
caaatgttgt tagccaagct acttcttcaa cagctgtatc tgcttcaaag ccgactgcct 780
ctccttcaag cattgcagca aacaattgta ctgtgaatac gtcacatatt gcaacgtctt 840
caatgaaggg tcttacgact acaggaaact cgtctcttaa tagcacatct aacactaaag 900
tatcagcagc gcctacaaat atggctgcca agaaaacatc tacccccata ataaattttg 960
ttggtggtta taagctgcag tcaacaggaa ataaagcaga agacacaaaa ggaaccgaat 1020
gtgttaaaag tactcctgtc acttctgtgt tgcagattcc tgaagtaaag caagacacag 1080
tgtcagaacc agtcacacct gcattctctg ctgctttaca gagtgatgtg cagccagtg 1140
gccatgatta tgtggaagag gtacgaaatg atgaaggaaa agtaattcgg ttccattgta 1200
aattatgcga gtgcagcttt aatgatccca atgctaagga gatgcactta aaagggcgaa 1260
gacacagact tcaatataaa aaaaaagtaa atccagattt gcaagtagaa gtaaaagccta 1320
gtattcgagc aagaaagatt caagaagaga aaatgaggaa gcaaatgcag aaggaggagt 1380
actggcgaag acgagaagaa gaggagcgtt ggagaatgga aatgagacgt tatgaagagg 1440
acatgtactg gaggagaatg gaggaagaac aacatcattg ggatgatcgc gcccgaaatgc 1500
cagatggagg ttatcctcat ggtcctccag gccatttagg cttcttgga gtccgaccag 1560
gcatgcctcc tcagcctcag gggcctgcac ccttacgtcg tctgactca tctgatgacc 1620
gttatgtaat gacmaaacat gccaccattt atccaactga agaggagtta caggcagttc 1680
agaaaattgt ttctattact gaacgtgctt taaaactcgt ttcagacagt ttgtctgaac 1740
atgagaagaa caagaacaaa gagggagatg ataagaaaga gggaggtaaa gacagagcct 1800
tgaaaggagt ttgctgagtg ggagtatttg caaaaggatt acttctccga ggagatagaa 1860
```

```

atgtcaacct tgttttctg tgctcagaga aaccttcaaa gacattatta agccgtattg 1920
cagaaaaacct acccaaacag cttgctgtta taagccctga gaagtatgac ataaaatgtg 1980
ctgtatctga agcggcaata attttgaatt catgtgtgga acccaaatg caagtcacta 2040
tcacactgac atctccaatt attcgagaag agaacatgag ggaaggagat gtaacctcgg 2100
gtatggtgaa agaccaccg gacgtcttg acaggcaaaa atgccttgac gctctggctg 2160
ctctaccca cgctaagtgg ttccaggcta gagctaattg tctgcagtc tgtgtgatta 2220
tcatacgcat tcttcgagac ctctgtcagc gagttccaac ttggtctgat tttccaagct 2280
gggctatgga gttactagta gagaaagcaa tcagcagtc ttctagccct cagagccctg 2340
gggatgcact gagaagagtt tttgaatgca tttcttcagg gattattctt aaaggtagtc 2400
ctggacttct ggatccttgt gaaaaggatc cctttgatac cttggcaaca atgactgacc 2460
agcagcgtga agacatcaca tccagtgcac agtttgatt gagactcctt gcattccgcc 2520
agatacacia agttctaggc atggatccat taccgcaaat gagccaacgt ttaacatcc 2580
acaacaacag gaaacgaaga agagatagt atggagtga tggatttgaa gctgagggga 2640
aaaaagacia aaaagattat gataactttt aaaaagtgtc tgtaaatctt cagtgttaaa 2700
aaaacagatg cccatttggt ggctgttttt cattcataat aatgtctaca ttgaaaaatt 2760
tatcaagaat ttaaaggatt tcatggaaga accaagtttt tctatgatat taaaaaatgt 2820
acagtgttag gtattatttg aatggaaaga cacccaaaaa aaaaaatgtg ctccgactag 2880
ggggaaaaca gtagttccga ttttttccca ttatttttat tttattttct ggttgccctc 2940
gcttccccc ctatttttgt gtcttttatt aactagtga ttgtcttatt aaatcttcac 3000
tgtatttaat gcaggatgtg tgcttcagtt gctctgtgta tttgatatt ttaatttaga 3060
ggttttgttt gctttttgac actagtgtga agttactttg ttatagatgg tatcctttac 3120
cccttcttaa ttttttacag cagtacgttt ttttgaacg tgagactgca gagtttgttt 3180
ttctatatgt gaaggattac aacacaaaaa gttatcctgc cattcgagt ctcagaactg 3240
aatgtttctg cagatcttgt ggcatttgtc tctagtgtga tatataaagg tgtaattaag 3300
acagagttct gttaatctaa tcaagtttgc tgtagttgt gcattagcag tataaaagct 3360
aatatatact atatggtctt gcaacagttt taaagcctct gcataattga taataaaaat 3420
gcatgacatt cttgttttta atagactttt aaaatcataa ttttaggttt aacacgtaga 3480
tctttgtaca gttgactttt tgacatagca aggccaaaaa taactttctg aatatttttt 3540
tcttgtgtat aagtggaaaag ggcatttttc acatataagt gggctaacca atattttcaa 3600
aagaacttca tcattgtaca actaacaaca gtaactagcc cttaattatg gtgacagttc 3660
cttattggtg tgtgtgagat tactctagca actattacag tataacacag atgatcttct 3720
ccacacaccc catcacccag ataatttaca gttctgttaa cagtgaggtt gataaagtat 3780
tactgataaa aaattatcta aggaaaaaaa cagaaaatta tttggtgtgg ccatcttacc 3840
tgcttatgtc tcctacacia agctaaatat tctagcagtg atgtaatgaa aaattacatc 3900
ttactgttga tatatgtatg ctctggtaca cagatgtcat tttgtgttca cagcactaca 3960
gtgaaataca caaaaaatga aattcatata atgacttaaa tgtattatat gttagaattg 4020
acaacataaa ctacttttgc tttgaaatga tgtatgcttc agtaaatca tattcaaat 4080
taaaaaaaaa aaaaaaaaaa actcga 4106

```

<210> 314

<211> 532

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (497)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (498)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (502)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (524)

<223> n equals a,t,g, or c

<400> 314

```
gactggaccc gggagacatc acagcgctgg gctaggggcg cggcttgaac tcgcctaaag 60
agctgcgccc tctcaccggt gccgccccag cgcgtgccgc ctgcaccgga cccggagccg 120
ccatgcccac gtgtcccaag tgcaacaagg aggtgtactt cgccgagagg gtgacctctc 180
tgggcaagga ctggcatcgg ccctgcctga agtgcgagaa atgtgggaag acgctgacct 240
ctggggggcca cgctgagcac gaaggcaaac cctactgcaa ccacccctgc tacgcagcca 300
tgtttggggc taaaggcttt gggcggggcg gagccgagag ccacactttc aagtaaacca 360
ggtggtggag accccatcct tggctgcttg cagggccact gtccaggcaa atgccaggcc 420
ttgtccccag atgccagggt ctcccttggt gccctaatag ctctcagtaa acctgaacac 480
ttggaaaaaa aaaaaanngg gnggcgtttt aaagattcct cgangggggc aa 532
```

<210> 315

<211> 1938

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1270)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1455)

<223> n equals a,t,g, or c

<400> 315

```
gcggctttgg ctctgggcga ggcggcgggg ccgggggcttc tcggacgagg cgggcttggc 60
gggcgcccgg cagctacagc tgcaggaggc ggccggcgac cccgacgcgc cgcccaagaa 120
gcggctgcgg gcagccgagg cgcccgaggc ggccggcgcg gcggcgggcg ccggcagcgg 180
gaaactggag gagcggtctt actcgggtgt gtgtgcacc gtgtcctgga cctgcccacg 240
gcctccgtgt accagtgtac taatggtcac ttgatgtgcg ctggctgttt tatccaccta 300
ctagcagatg cccggctgaa ggaggagcag gccacgtgcc ccaattgtcg ttgtgagatc 360
agtaagagcc tctgctgccg gaacctggcc gtggagaaag ccgtgagcga gctgccttca 420
gagtgtggct tctgcctgcg ccagtgtccc cgctccctcc tggagaggca ccagaaagag 480
gaatggcacg gacagggtaa cccagtgcga gtacaaacgc atcggctgcc catggcacgg 540
ccccttccat gagctgacgg tgcacgaggc tgcgtgcgcc caccggacca agacaggcag 600
tgagctgatg gagatcctgg atgggatgga ccagagccac cgcaaggaga tgcagctgta 660
```

caacagcatc ttcagcctgc tcagcttcga gaagattggc tacacagagg tccagttccg 720  
gccgtaccgc acagacgact tcatcacgcg cctgtactat gagacgcca gggtcacagt 780  
gctgaaccag acgtgggtcc tgaaggctcg agtcaacgac tcggagcgta accccaacct 840  
gtcctgcaag cgtacgctct ccttcagct cctcctcaag agcaaggta cggcaccgct 900  
ggagtgtctc ttcctgtctc tcaagggtcc ctacgacgac gtgaggatca gccccgtcat 960  
ctaccacttt gtcttcacca acgagagcaa cgagacggac tacgtgccac tgcccatcat 1020  
tgactccgtg gagtgaaca agctgctggc tgccaagaac atcaacctgc ggctcttctt 1080  
gttccagata cagaagtagg gcggggcctc aggatgtccg aggagcccac gggcggcac 1140  
ccagcaccgc tgccctgtcc acctggctgg cagctgcttc acaggactat ctgatcactt 1200  
tagcaaagga ggagaacaaa cgaagccaac acagggcaag tctgcatgcy tgcgcgacgg 1260  
ggcccccgcn tccggctcac cccccgacc cctgcctccc ctcttccga gggccgccag 1320  
aggtgtgggt gacccgaaga ggagacggtg caccaggcgc cccgaggcta agagacggtg 1380  
gcagcaagga ggccgagagg cacagcgacc ctgccccagc ccttctgtgc agtcaggcgg 1440  
cgtgtgtgtc ccatnctgcy ggttccggcy gggcgcgggg gccttgtctg catcagacgg 1500  
gatatccgaa tatctgatag caattaaag gcagccttgt ttcgtacttt ctgttttgtt 1560  
cgaggggaag gcatggctgt gaatggacag cgtgggggct ttggtttggt ctgggggtca 1620  
gagcctgccc cgccccatc tgtgtgcccg cacacgtccc ccgaggaaag actcagagac 1680  
actgcctccc cctacgctct gtcattgggt cttgagactg aggcttgggc aggaagatcc 1740  
aggtagggtc ggggtgccc tgccaaccgg ccgctcccag ggagacagga ctcagccacc 1800  
agggctcagc aggcattttc ggaaagcagg gtgaaattgt ctcttcccag gaaaaagatt 1860  
aaactccttg caggctcttg gataagttac acaaaaaaaaa aaaaaaaaaa ggcgcccgt 1920  
cgcgatctag aactagtc 1938

<210> 316

<211> 818

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (55)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (814)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (818)

<223> n equals a,t,g, or c

<400> 316

gcggccgccc ggcgccccca gcagcccag cggggcgca cagccggggc gcagncgcgc 60  
ccccgcgc gattgacatg atgtttccac aaagcaggca ttcgggctcc tcgcacctac 120  
cccagcaact caaattcacc acctcggact cctgcgaccg catcaaagac gaatttcagc 180  
tactgcaagc tcagtaccac agcctcaagc tcgaatgtga caagttaggc agtgagaagt 240  
cagagatgca gcgtcactat gtgatgtact acgagatgtc ctacggcttg aacatcgaga 300  
tgcacaaaca ggctgagatc gtcaaaaggc tgaacgggat ttgtgcccag gtcctgcctt 360  
acctctccca agagcaccag cagcaggctt tgggagccat tgagagggcc aagcaggatca 420

250

ccgctcccgga gctgaactct atcatccgac agcagctcca agcccaccag ctgtcccagc 480  
tgcaggccct ggccctgccc ttgacccac taccggtggg gctgcagccg ccttcgctgc 540  
cggcggtcag cgcaggcacc ggcctcctct cgtgtgccgc gctgggttcc caggcccacc 600  
tctccaagga agacaagaac gggcacgatg gtgacacca ccaggaggat gatggcgaga 660  
agtccgatta gcagggggcc gggacaggga ggttgggarg ggggacarag gggagacaga 720  
ggcacggaga gaaaggaatg tttagcaca gacacagcgg agctcgggat tggctaaayt 780  
ccatagtatt atgktggccc gggggggggc ccancan 818

&lt;210&gt; 317

&lt;211&gt; 837

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 317

gggcacgagc gacatggagc tggtcctcgc gggccgcccg gtgctggtea ccggggcagg 60  
caaaggtata gggcgcgcca cgggccaggc gctgcacgcg acgggcgcgc ggggtggggc 120  
tgtgagccgg actcaggcgg atcttgacag ccttgctcgc gagggtcccg ggatagaacc 180  
cgtgtgcgtg gacctgggtg actgggaggc caccgagcgg gcgctgggca gcgtggggcc 240  
cgtggacctg ctgggtgaaca acgccgctgt cgcctgctg cagcccttcc tggaggtcac 300  
caaggaggcc tttgacagat cctttgaggt gaacctgcgt gcggtcatcc aggtgtcrca 360  
gattgtggcc aggggcttaa tagcccgggg agtcccaggg gccatcgtga atgtctccag 420  
ccagtgtcc cagcgggcag taactaacca tagcgtctac tgctccacca aggggtgcct 480  
ggacatgctg accaaggtga tggccctaga gctcggggcc cacaagatcc gagtgaatgc 540  
agtaaaccac acagtgggtg tgacgtccat gggccaggcc acctggagtg acccccacaa 600  
ggccaagact atgctgaacc gaatccact tggcaagttt gctgaggtag agcacgtggt 660  
gaacgccatc ctctttctgc tgagtgaccg aagtggcatg accacgggtt ccactttgcc 720  
ggtggaaggg ggcttctggg cctgctgagc tccctccaca cacctcaagc cccatgccgt 780  
gctcatccta ccccaatcc ctccaataaa cctgattctg ctgccccaaa aaaacga 837

&lt;210&gt; 318

&lt;211&gt; 1448

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (878)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1198)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1395)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature



&lt;222&gt; (1397)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1445)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 318

```

gggtctggag agcaggactg ggtcaacagg cccaagaccg tgcgcgacac gctgctggcg 60
ctgcaccagc acggccactc ggggccttcg agagcaagtt taagaaggag ccggccytga 120
ctgcaggcag gttgttggtt ttcgaggcca acggggccaa cgggtctaaa gcaggtaggg 180
gcggctgtga agtgaggggg tctaggggag aaaaggggac ggagagcaga ggaaggggtg 240
ttctttggat tcaccatttt accccagccc agaaacaaca aacaccccac ttcctgatct 300
cctgagggcg aaccagtgtt tgggtggcaac gtgttcacgt ctgaagcagc ataacaaaga 360
atgagtcaga ctgggctgat acgctctgaa cacggggttt tcctttccca gcacattctt 420
ggatgggagc atgagggcac cagtcacctt twaacctatt gggggacatt agcagtcaca 480
tggtgagtg c aaacgaggtta cttttgtgca tgtktaaaa caggcagtta caagcgtgtc 540
atthtcagt gctccatttt aaatcagtct gctgcctcag aatcccgtac gcctgaaggt 600
tttaagttgc atgtgcacct gaaactcgta tatgagtatt ttctgtctgt gcttttagag 660
aggaggaatt ctgtaacgac ttttgtttcg ggtaggaag agaattgatct ctttcagtgc 720
accgccactt atgttacctt tttcctttta tttctttgtg tttccagttg caagaacagc 780
aaggaaaagg aagccctctc cagaaccaga aggtgaagtc gggcccccta agatcaacgg 840
agagggccag ccgtggstgt ccacatccac agaggggntc aagatcccca tgactcctac 900
atcctctttt gtgtctccgc caccaccac tgctcacct cattccaacc ggaccacacc 960
gcctgaagcg gcccagaatg gccagtcccc catggcagcc ctgatcttag tagcagacaa 1020
tgacaggggc agtcatgcct caaaagatgc caaccaggtt cactccacta ccaggaggaa 1080
tagcaacagt ccgccctctc cgtcctctat gaaccaaaga aggctggggc ccagagaggt 1140
ggggggccag ggagcaggca acacaggagg actggagcca gtgcaccctg ccagcctncc 1200
ggacttctct ctggcaacca gtgccccgct gtgctgcacc ctctgccacg agcggctgga 1260
ggacaaccat tttgtgcagt gccgtccgtc ctttgacaag ttctcttcct tgctcagaca 1320
aagataaaca gagggagtag tgagaggctt ttccagtggt gaaaatgcct ctgtgggtca 1380
atgtccctgg gcttntnaag gggaattcaa catcttcttg ggtgtaagtg aaaaaaaaaa 1440
aaacntgg                                     1448

```

&lt;210&gt; 319

&lt;211&gt; 1493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 319

```

tcgaccacag cgtccggaag taatgatgac aaaatactct aacctttcct tggagagtca 60
taacttctcg ctgactgctt cacctcttac aagtctgccc atcccggaag taatgatgac 120
aaaatactcc aaccttttct tggaaagtca taacatctca ctgactgaac attccagtgt 180
gccagtggaa aaaaatatca ctttagaacg accttctgct gtagaactca catgtcagtt 240
cacaacttct ggggatgtga attcagtaaa tgtgacttgg aaaaaagggg atgaacaact 300
taagaattac catgtcagtg ccacagaagg catcctgtat acccagtaca agttttccat 360
cattaatagc gaacaactgg gaagctattc ttgtttcttt gaagaggaaa aggaacgaag 420
gggcacattt aatttcggag tccctgaagt tcagagaaaa aacaaaccat tgatcactta 480
tgtgggggat tccgttgtct tgggtgtgaa atgccgacac tgtgctcctt taaattggac 540
ctggtacagt ggtaatagga gtgtacaggt tcctcttgat gttcacatga atgaaaagta 600

```

```
tgcgatcaat ggaacaaacg cgaatgaaac aaggcttaag ataatgcagc tttcagaaga 660
cgataaagga tcttattggt gccatgcaat gttccagttg ggcgagagcc aagaaagtgt 720
tgaactgggt gtgataagtt atttggtgcc cctcaaacca tttcttgaa tagttgttga 780
agttattctt ttagtggtta ttattctggt ttgtgaaatg cacacccaaa agaaaaagat 840
gcacatggat gatgggaaag aatttgaaca agttgaacag ttgaaatcag acgatagcaa 900
cggcatagaa aataatgccc ccaggcacag aaaaaatgaa gctatgagcc agtgaaagca 960
aaacatcgtg tcaagagtaa tgggaagatg tatagtttct acttcagctt tgtttatggt 1020
tcctgtgaag aacatctgag tttttatttt tacaaggatg aaaagtttat gtgatatgct 1080
cagcagtagt tttgcaataa tacctgctat ctcagatcca aagatatatt ttccttctgt 1140
gattatttta cattaaagca aggtaaatca tattaatat gttctatgag ctataacca 1200
ggataactaa tttcatcttg gtcatacagg gatgcacaga agagatacca gcaaaaccag 1260
ttagtagtac atgaactaat gtcattcaag acctgcgtat aaccaaagaa ttcattaaag 1320
agaaaacttt tttgccattt gccttgkttt tttttctaata tatgcttact atgtgtagaa 1380
atatttgtaa taattttcat gtaatgkta cccctctgtca tattggataa aaacatcttt 1440
attaagaaat gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaagggcgcc cgc 1493
```

<210> 320

<211> 609

<212> DNA

<213> Homo sapiens

<400> 320

```
ggcacgagtg gcttctgacc ctttcttccg ccactaccgc cagctcaatg agaagctagt 60
gcagctcatc gaagactata gccttgtctc ctttatccct ctcaacatcc aggacaagga 120
gagcatccag cgagtcctgc aggctgtgga taaagccaat ggatactgtt tcggagccca 180
agagcagcga acttggaagc catgatgtct gccgcaatgg gagccgactt ccatttctct 240
tccacactgg gcatccagga gaagtacctg gcaccctcga accagtcagt ggagcaggaa 300
gccatgcagc ttagcaaca aggtggaccc tggagagcag gatgcataat ccagcactgg 360
ggaaagtgga ggctcctgat gcaggctgca gacccaagag caagtcctcc cagccagagc 420
tggcgggctg gcaaggggat attcagctct gcaaaggact tctggccaaa aagccagaca 480
tggtgccaag cagaacaccc cccatactgt cagtgggtgc cgtgagctct ggccctgcca 540
ccagaaagtc gagcactggg cctagtcagg ctgtgatgaa atgtgctaca atacaagagt 600
ttattttct
```

<210> 321

<211> 502

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (458)

<223> n equals a,t,g, or c

<400> 321

```
tagtggatcc cccgggctgc aggaattcgg cagcagcaga gcttcgctct tgctgetccc 60
ctgaggtgaa ctgaagccag cagccccgca tcatgtcaaa gctcggccgg gccgcccggg 120
gcctcaggaa gcccgaggtc ggcggtgtra tccgggcgat cgtgcgggca ggccctggcca 180
tgcccgggcc ccactaggc ccagtgtctg gtcagagagg cgtttccatc aaccagtttt 240
gcaaaggagt caatgagagg acaaaggaca tcaaggaagg cattcctctg cctaccaaga 300
tttttagtgaa gcctgacagg acatttgaaa ttaagattgg acagccact gtttcctact 360
```

253

tcctgaaggc agcagctggg attgaaaagg gggccccggca aacagggaaa gaggtggcag 420  
gcctggtgac cttgaagcat gtgtatgaga ttgcccgnat caaagctcag gatgaggcat 480  
ttgcctgcag gatgtacccc tg 502

&lt;210&gt; 322

&lt;211&gt; 2630

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1952)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 322

gggcatccag agtacgggtc gagccccggc catggagccc ccctggggag gcggcaccag 60  
ggagcctggg cgccccgggc tccgccgcga ccccatcggg tagaccacag aagctccggg 120  
acccttcagg caccctctgga cagcccagga tgctgttggc caccctctc ctcctcctcc 180  
ttggaggcgc tctggcccat ccagaccgga ttatttttcc aaatcatgct tgtgaggacc 240  
ccccagcagt gctcttagaa gtgcagggca ccttacagag gcccttggtc cgggacagcc 300  
gcacctcccc tgccaactgc acctggctca tcttgggcag caaggaacag actgtcacca 360  
tcaggttcca gaagctacac ctggcctgtg gctcagagcg cttaaccta cgctccctc 420  
tccagccact gatctccctg tgtgaggcac ctcccagccc tctgcagctg cccgggggca 480  
acgtcaccat cacttacagc tatgtctggg ccagagcacc catgggccag ggcttcctgc 540  
tctcctacag ccaagattgg ctgatgtgcc tgcaggaaga gtttcagtgc ctgaaccacc 600  
gctgtgtatc tgctgtccag cgctgtgatg ggggtgatgc ctgtggcgat ggctctgatg 660  
aagcagggtg cagctcagac cccttccttg gcctgacccc aagaccgctc ccctccctgc 720  
cttgcaatgt caccctggag gacttctatg gggctctctc ctctcctgga tatacacacc 780  
tagcctcagt ctcccamccc cagtcctgcc attggtgctg gaccccatga tggccggcgg 840  
tggccgtgag cttcacagcc ctggamtgg gctttggaga tgcagtgcag gtgtatgacg 900  
gccctggggc ccctgagagc tcccgaactac tgctgtagtct caccacttc agcaatggca 960  
aggctgtcac tgtggagaca ctgtctggcc aggtctgtgt gtccctaccac acagtgtctt 1020  
ggagcaatgg tcgtggcttc aatgccacct accatgtgag gggctattgc ttgccttggg 1080  
acagaccctg tggttaggac tctggcctgg gagctggcga aggcctaggt gagcgtgct 1140  
acagtggagg acagcgctgt gacggctcat gggactgtgc tgacggcaca gatgaggagg 1200  
actgcccagg ctgcccacct ggacacttcc cctgtggggc tgetggcacc tctggtgcca 1260  
cagcctgcta cctgcctgct gaccgctgca actaccagac tttctgtgct gatggagcag 1320  
atgagagacg ctgtcgccat tgccagcctg gcaatttccg atgccgggac gagaagtgcg 1380  
tgtatgagac gtgggtgtgc gatgggcagc cagactgtgc ggacggcagt gatgagtggg 1440  
actgctccta tgttctgccc cgcaagggtca ttacagctgc agtcattggc agcctagtgt 1500  
gcggcctgct cctggtcatc gccctgggct gcacctgcaa gctctatgcc attcgcaccc 1560  
aggagtacag catctttgcc cccctctccc ggatggaggc tgagattgtg cagcagcagg 1620  
caccctcttc ctacgggcag ctcatgtccc aggttgccat cccacctgta gaagactttc 1680  
ctacagagaa tcctaattgat aactcagtgc tgggcaacct gcgttctctg ctacagatct 1740  
tacgccagga tatgactcca ggaggtggcc caggtgcccg ccgtcgtcag cggggccgct 1800  
tgatgcgacg cctggtacgc cgtctccgcc gctggggctt gctccctcga accaacaccc 1860  
cggtctgggc ctctgaggcc agatcccagg tcacaccttc tgctgctccc cttgaggccc 1920  
tagatggtgg cacaggtcca gccctgagg gnggggcagt ggggtgggcaa gatggggagc 1980  
aggcaccccc actgcccata aaggtcccc tcccatctgc tagcacgtct ccagccccca 2040  
ctactgtccc tgaagcccca ggccactgc cctcactgcc cctagagcca tcaactattgt 2100  
ctggagtggg gcaggccctg cgaggccgcc tgttgcccag cctggggccc ccaggaccaa 2160

```

ccccggagccc ccctggaccc cacacagcag tcctggccct ggaagatgag gacgatgtgc 2220
tactggtgcc actggctgag ccgggggtgt gggtagctga ggcagaggat gagccactgc 2280
ttacctgagg ggacctgggg gctctactga ggctctccc ctgggggctc tactcatagt 2340
ggcacaacct tttagagggt ggtcagcctc ccctccacca cticcttccc tgtccctgga 2400
tttcagggac ttggtgggccc tcccgttgac cctatgtagc tgctataaaag ttaagtgtcc 2460
ctcaggcagg gagagggtc acagagtctc ctctgtacgt ggccatggcc agacacccca 2520
gtcccttcac caccacctgc tccccacgcc accaccattt ggggtggctgt ttttaaaaag 2580
taaagttcct agaggatmaw aaaaaaaaaa aaaaaaaaaa aaaaaaaagg 2630

```

<210> 323

<211> 1874

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (67)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1735)

<223> n equals a,t,g, or c

<400> 323

```

tcgacccacg cgtccggccg gggcgccctc cggaagcttt tccaactttc cagaagtttc 60
tcgggagggg cgggaggagg ggaacgccat atatagacct ggagagccgg gagcgcgagg 120
agtggaatcg gtccgcggct cgagtgggtc tctagtccgg cgccagccgc ccggcccagc 180
cctcacaggt ccttcgtggt gcataaccatc cgctcccag ccatgcgctt cctcctgctt 240
accagcactt gctgctcct ggccatggcc ctggctgccc aggtgaagaa gccagcggcc 300
ccaggcacag cagagaagct garcccaaaa ggggccacgc tggcagagcg cagtgtggc 360
ctggccttca gcctgtacca ggccatggcc aaggaccagg cgggtggagaa catcctgctg 420
tcgcctgtgg tgggtggcctc atccctgggg ctgtgtcgc tggggggcaa ggccaccaca 480
gcgtcccagg ccaaggcggt gctgagtgca gacgagytgc gtgatgagga ggtgcacgcg 540
ggsctkggcg agytgttgcg agctttcagc aacagcacgg cgcgcaacgt gacctgaagc 600
tgggcagccg cctgtatggg ccagctcgg tgarcctcgc ggaggacttt gtgcgcagca 660
gcaagcagca ctacaactgc gagcactcca agatcaactt ccgcgacaag cgcagcgcgc 720
tgcagtccat caatgagtgg gccgcacaga ccaccgatgg caagctgcct gaggtcacca 780
aggacgtgga gcggacggat ggcgcgctgc tgggtcaacgc catgttcttc aagccgcact 840
gggacgagaa gttccaccac aagatggtgg acaaccgagg ctcatggtg acccgctcgt 900
ataccgttgg ggttacgatg atgcaccgca caggactcta caactactac gacgacgaga 960
aggagaagct gcagatggtg gagatgcccc tggcccacaa gctgtccagc ctccctcatcc 1020
tcatgcccga ccacgtggag cccctggagc gcctggagaa gcttctgacc aaggagcagc 1080
tgaagatctg gatggggaag atgcagaaga aagccgtcgc catctccttg cccaaggggg 1140
tggtagaggt gaccacacgac ctgcagaaac acctggctgg actgggtctg actgaggcca 1200
tcgacaagaa caaggcagac ctgtcacgca tgtcaggcaa gaaggacctg tacctggcca 1260
gcgtgttcca cgctaccgcc ttcgagtggg acacagaggg caaccctttt gaccaggaca 1320
tctacgggcg tgaggagctg cgcagtccca agytcttcta cgctgaccac cccttcattt 1380
tcctggttcg agacacccag accggtccc tgctgttcac tgggcgcctg gtccggccca 1440
agggtgacaa gatgcgagat gagctgtagg gcccagggga tggcaggagg cagcccaagg 1500
ctcctgagac acatgggtgc tatggggggt agctgaggta ccgaccttgg atgtgcatg 1560

```

gggtgggggt gggaaaacag agcaggcttc ctggatgtct gagcagatct tcccaggcag 1620  
aattgactct gtctggatgt gggcccccag ataccgtgat gctgagcccg gacacscac 1680  
attctgrggr ccctgggggc agttggcgtg tcttgccctc agcatcctgg gattnaagcc 1740  
tgcccttcaat cagtgttcat atttatagcc aagtgccttc tcatctgtga gacagaatcg 1800  
agctargggg cttcagccca gccctgtgga atggggaccg tcttttcctt accctaccat 1860  
cacctcagcc ctaa 1874

<210> 324

<211> 2325

<212> DNA

<213> Homo sapiens

<400> 324

aagaaatgca gatgagtgt aaacatctgt tctcaattat gttgatctgt gtgcgcagta 60  
ctggagcatt taccatttca tgttgagcct caaatgcttg ttttctgggg tccacaaaag 120  
acagttttat acattttgag ttgttcataa agtttgcctt gtgatatgcc tggcacttaa 180  
agacaaatth ttctggtagt aaaagttcag atttattact atgtcatgaa acacagtaca 240  
ttcaaatcaa acggcagttt tctttctaag taaatgattt ccagtcactt aaaagggtggg 300  
caagatgaga taaagacatt ttgatacagt aattgttttg gttgggtttt catgtcagtt 360  
tatgtttgac taaagctctc ttcatatgca gggttataaa tttgttaggt ctgttgctcc 420  
atgattaaac atgsagtgcc tcctctctga tttaatattc tgcaggtcac tgtaacctgc 480  
taggcaaaagt cacaacattg cattaaagag gtgatatgctt tgctaataac actgttttaa 540  
aggacgtaca gttaaaggaa tattaagtgg gagaaagcct acaaggcttt tagaatatta 600  
tcagtatctt cttttctggt attcagatgt tatgtgataa aacacatttt ttttgctttt 660  
cccagataca ctatatattt gttcaagggt aaatctataa aatgtatata ctttattttg 720  
tggttttgct atttataaat ttaatgtttt aactgttgct catttatggt ttgttttggg 780  
tggtggtggt catctgtata tcaccatggt aatttgtaat ggaagtgcac ttcgtagtgt 840  
atattgttac tgacattaaa atactttata gcattgtctc tgagcaaaaag ctagtattta 900  
attgtacaaa tgaataagca agttacatgt tattgtttgc tcttgacagg gtaggcctct 960  
taaaagaaaa aaaacaactt gttttttctt tatgaatccc ctatgccaaa cacatacctt 1020  
ccatgcatga catgagatct gcaaaactgga ttttagccac cgtattttatt tagtcaaaaa 1080  
aattgtccat tgtagcagac ccgaaaaacct ttttgctgtg acatgaaacc atgttattct 1140  
tatcttctta aaacacagcc tgggatggaa tgccatggc atttttttca gagaacatcc 1200  
tttatctgct atgactgaat ccttaggaaa tgtaagctat aaccctttga ttttcaagaa 1260  
ctaccgaata agtgtatgaa gaggtgggtt tttaaaactt caagttggaa tttttatgag 1320  
gtcactgtgt aatttgaaga attgtgtgag attgtcatga tataaattcc ttttaaggac 1380  
tgataaatag aatgaaaagt ttccaggtag tttaaaactc cacaggtcag tttccttttc 1440  
attcctgctt cactgtggtt tataagccta cgggagagca ccgttgctca gatgctactg 1500  
tgagcttcct gtccggtgtt agaaaagtaac tagttaaag ttcatttttag aatgtatggt 1560  
ttttggggat gaactaagaa ttagttatta gttccaaagg actgagaacc aattttaata 1620  
ttttcacatt tataggaaag aaattcatat gtccctgaaa cttctaggac aaaaccaaac 1680  
aagtaaggag ggaactgttg caaagccatt tcatcgagaa ggggacagaa ggagaaatac 1740  
acacatgtat acacaaacag aatggttgag aaaacgtttt aataaaatgt gaggtttgta 1800  
tgtgtgcgtg tatatattht cacttaacct ctaaaattct cttctacagt atctctgtta 1860  
tgaatatgat ggaagcaaa cattttggtg gtgagactat tgttaaaata aatttgagaa 1920  
agacgaaaaat tttgtgagtc ttgataatta caagtcaaca gctatcgaaa gttagcacag 1980  
cttgtctgtg gtgctgtttt tttccctact gcagtggact tatgctgttt tcatgttttag 2040  
aaacaaaaag gtttcatgtg attcatgtgt aagatgcaca gtatttgaca tcctgattat 2100  
gtaatcccta ttccatctat ccagtcttac acttatggtt ggcctcaaat ctattgcatt 2160  
tatgataatg tattatatct agttgagttt aatatttttt tattagcctg taaataaaga 2220  
tggcatcttc tacattaaaa tgatattgat ctcatttttt taaataaaca ttttgtttcc 2280

ttgacgttaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 2325

<210> 325

<211> 785

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<400> 325

```
ggcctncggc aaagaagcat agccacgggg ccamagccag gtgtgtcctt gcagttggaa 60
cccaggagtt ccggaagcca aagccccccc acgagggtcc cgcaagacc tggtagcgga 120
ggagagcccc gagctgctga accctgagcc caggagactg agcccagagt tgaggctact 180
gccctatatg atcactctgg ggcacgccgt gcacaacttc gccgacgggc tggccgtggg 240
cgccgccttc gcgtcctcct ggaagaccgg gctggccacc tcgctggccg tgttctgcca 300
cgagttgcca cagcagctgg gggacttcgc cgcttgctg cagcgggggc tgtccgtgcg 360
ccaagcactg ctgctgaacc tggcctcgcg gctcacggcc ttcgctggtc tctacgtggc 420
actcgcggtt ggagtcagcg aggagagcga ggctggatc ctggcagtgg ccaccggcct 480
gttcctctac gtagcactct gcgacatgct ccgggcgatg ttgaaagtac gggaccgcg 540
gccctggctc ctcttcctgc tgcacaacgt gggcctgctg ggcggctgga ccgtcctgct 600
gctgctgtcc ctgtacgagg atgacatcac cttctgatac cctgccctag tccccacct 660
ttgacttaag atcccacacc tcacaaacct acagcccaga aaccagaagc ccctatagag 720
gccccagtcc caactccagt aaagacactc ttgtccttgg aaaaaaaaaa aaaaaaaaaa 780
aaaaa 785
```

<210> 326

<211> 244

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (244)

<223> n equals a,t,g, or c

<400> 326

```
aatcactaaa ggaaaaayag tagcctgcag taccgggtccg gaattcccgg gtcgacccac 60
gcgtccgacg acagaagggg acggctgcga gaagacgaca gaagggtagc gctgcgagaa 120
gacgacagaa gggtagcggt gcgagaagac kacagaaggg tacggctgcg agaagackac 180
agaagggtag ggctgcgaga agacgacaga aggtacggct gcgagaagac gacagagggt 240
acgn 244
```

<210> 327

<211> 2454

<212> DNA

<213> Homo sapiens

<400> 327

```

gctgcggcgg ggtctggggc gcagagcagc ggcgggagga ggcggacacg tggcaacagc 60
ggtacagccc gggcggcggc acaacagcgg cggcggcatc ggcccagcgg ccggccgccc 120
tcccaccctc ccgcccgcgg gcagccctag ctccctccac ttggctcccc tgggtcccgt 180
cgctcggccg ggaagctgctc tgtgcttttc tctctgattc tccagcgaca ggacccggcg 240
ccggcactga gcaccgccac catggggaag ggggttggac gtgataagta tgagcctgca 300
gctgtttcag aacaaggtga taaaaagggc aaaaagggca aaaaagacag ggacatggat 360
gaactgaaga aagaagtttc tatggatgat cataaactta gccttgatga acttcacgt 420
aaatatggaa cagacttgag ccggggatta acatctgctc gtgcagctga gatcctggcg 480
cgagatggtc ccaacgccct cactccccct cccactactc ctgaatggat caagttttgt 540
cggcagctct ttgggggggt ctcaatgtta ctgtggattg gagcgattct ttgtttcttg 600
gcttatagca tccaagctgc tacagaagag gaacctcaaa acgataatct gtacctgggt 660
gtggtgctat cagccgttgt aatcataact ggttgcttct cctactatca agaagctaaa 720
agttcaaga tcatggaatc cttcaaaaac atggtccctc agcaagccct tgtgattcga 780
aatggtgaga aaatgagcat aaatgcggag gaagttgtgg ttggggatct ggtggaagta 840
aaaggaggag accgaattcc tgctgacctc agaatcatat ctgcaaatgg ctgcaagggt 900
gataactcct cgctcactgg tgaatcagaa cccagacta ggtctccaga tttcacaat 960
gaaaaccccc tggagacgag gaacattgcc ttcttttcaa ccaattgtgt tgaaggcacc 1020
gcacgtggta ttgttgtcta cactggggat cgactgtga tgggaagaat tgccacactt 1080
gcttctgggg tgggaaggag ccagaccccc attgtgcag aaattgaaca ttttatccac 1140
atcatcacgg gtgtggctgt gttcctgggt gtgtctttct tcatccttct tctcatcctt 1200
gagtacacct ggcttgaggc tgctatcttc ctcatcggtt tcatcgtagc caatgtgccg 1260
gaaggtttgc tggccactgt cacggtctgt ctgacactta ctgccaaacg catggcaagg 1320
aaaaactgct tagtgaagaa cttagaagct gtggagacct tggggtccac gtccaccatc 1380
tgctctgata aaactggaac tctgactcag aaccggatga cagtggccca catgtggttt 1440
gacaatcaaa tccatgaagc tgatacgaca gagaatcaga gtggtgtctc ttttgacaag 1500
acttcagcta cctggcttgc tctgtccaga attgcaggtc tttgtaacag ggcagtgttt 1560
caggctaacc aggaaaacct acctattctt aagcgggcag ttgcaggaga tgcctctgag 1620
tcagcactct taaagtgcac agagctgtgc tgtggttccg tgaaggagat gagagaaaga 1680
tacgccaaaa tcgtcgagat acccttcaac tccaccaaca agtaccagtt gtctattcat 1740
aagaaccccc acacatcgga gccccaacac ctgttggtga tgaagggcgc ccagaaagg 1800
atcctagacc gttgcagctc tatcctcctc cacggcaagg agcagcccct ggatgaggag 1860
ctgaaagacg cctttcagaa cgcctatttg gagctggggg gcctcggaga acgagtccta 1920
ggtttctgcc acctctttct gccagatgaa cagtttcctg aagggttcca gtttgacact 1980
gacgatgtga atttccctat cgataatctg tgctttgttg ggctcatctc catgattgac 2040
cctccacggg cgcccggttc tgatgccgtg ggcaaatgtc gaagtgtctg aattaaggct 2100
atcatggtca caggagacca tccaatcaca gctaaagcta ttgccaaagg tgtgggcac 2160
atctcagaag gcaatgagac cgtggaagac attgctgccc gcctcaacat ccagtcagc 2220
caggtgaacc ccagggatgc caaggcctgc gtagtacacg gcagtgatct aaaggacatg 2280
acctccgagc agctggatga cattttgaag taccacactg agatagtgtt tgccaagacc 2340
tcccctcagc agaagctcat cattgtggaa aggctgccaa agacaggggt ctatcgtggg 2400
ctgtgactgg tgacggtgtg aatgactctc cagctttgaa gaaagccaga catt 2454

```

&lt;210&gt; 328

&lt;211&gt; 505

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (10)

&lt;223&gt; n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (15)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (182)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (189)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (246)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (300)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (302)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (332)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (335)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (339)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (342)  
<223> n equals a,t,g, or c



<220>  
<221> misc feature  
<222> (367)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (394)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (401)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (405)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (407)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (411)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (419)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (420)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (422)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (424)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (436)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (440)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (451)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (452)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (454)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (459)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (467)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (469)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (470)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (472)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (474)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (475)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (477)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (479)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (482)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (483)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (485)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (488)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (490)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (491)  
<223> n equals a,t,g, or c

<400> 328  
aattcgcan agggnagtgc gaagtagtgg gtgacttttg ttctctttct ggcagaactt 60  
tgcttacaca ttctactac ccctgggaat tctaactcag atgtgggtag cagcttctc 120

aaagagaaac tttttcccag ctgggtgctg tggctcacac ctgtgaatcc cagccctttg 180  
gnaggctgna gtgggcagat cgcttgagcc caggagtttg agatcagcct gggcaacatg 240  
gtgaantcca tctctgtgaa aaatacaaaa attagccagg tgtggtggtg cgcgcctgtn 300  
antcccagct actagggagg ctgaagggtg gnggnttgnt tnagcccagg aggttgaggc 360  
tgcattnggc tgggattcaa accatgttac tccntgacca ngtgngncct ntttcaaann 420  
angnaaggga aggggnaagn aaaggaaaag nngnaggng atgccgntnn tngnntngna 480  
gnngnatnan ntaaaaattt gggggg 505

<210> 329

<211> 559

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (335)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (343)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (373)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (385)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (387)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (441)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (445)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (448)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (457)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (473)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (487)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (503)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (505)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (551)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (553)

<223> n equals a,t,g, or c

<400> 329

```
nnanancctg ggaggcagag tttgcagtga gccgagatgg cgccactgca ctccagcctg 60
ggggacagag cgagactcca tctcaaaaaa aaaaaaaaaa aaaattaaaa attaatgttct 120
ttagttgcac tagccatatt tcaaatactt gatggataca tgtggctagt ggctaacata 180
agggatagca cagatataaa acatttcctc ccaaagtgtt gggattacag gcatgagcca 240
ccgcgcccgg cctatcatat gaattttgag ggaacacaat catgcagtct gtagcagatg 300
gtaataggct gatataattac acttgttgat gtaanctgga tangtttctt tcttctccaa 360
ggacagcttt ttnaatattht aacantncca ttaatttttc agtttccggg agaattttat 420
aatttataaat tgccgactta ngganaancc aattggncca accattacaa tanattttta 480
attccgntta aaaaatccca ccngnggggg aattccgctt aaaattttat tttccattat 540
tcccaatggc ntnaattta                                     559
```

<210> 330

<211> 467

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (99)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (125)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (135)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (138)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (145)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (256)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (263)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (275)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (298)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (305)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (330)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (341)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (344)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (391)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (393)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (398)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (402)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (422)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (428)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (440)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (441)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (453)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (456)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (458)  
<223> n equals a,t,g, or c

<400> 330  
aatnatgctc tgcgtgatga tgttgccgct ggtcgtcgtc ggttgccat caaagcagtc 60  
tgtcagtcag tgcgtgaagc caccaccgcc tccggtggna tgaatgcagc ctccccccga 120  
ctggncagac accgntgnaa cgggnattat ttcaccctca gagagaggct gatcactatg 180  
caaaaacaac tgggaggaaa cccagaagta tattgaatga gcagtgcaga ttagagttgc 240



267

ccatatcgat gggcancaat tgncaattat tgtgnagcaa tacacacggg gtttccangg 300  
gagtnntaaa tgccttaaag taattaaaaan ccgggggcaat nccntttttac ggatgttttg 360  
ctgggggtttc cgtttttaac caacattttt ntnggggncc gnccacaaat tttgggggttg 420  
gnattggncg ttttttcttn ntggcccat ttncngnaa acggggg 467

&lt;210&gt; 331

&lt;211&gt; 418

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (22)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (37)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (126)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (131)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (196)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (202)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (250)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (257)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

<221> misc feature  
<222> (284)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (298)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (338)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (344)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (353)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (380)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (387)  
<223> n equals a,t,g, or c

<400> 331  
gagctgccaa cctggcaatt antgtctgct aagggtncctc tttattcacc cttacttgga 60  
cttcctttcc tgtagggaat ctcacgtaaa atgaaatctt ccctcccca aggtgtccgc 120  
aatgtngcca ntgtctgtct gcagattggc tacccaactg ttgcatcagt accccattct 180  
atcatcaacg ggtacnaacg antcctggcc ttgtctgtgg agacggatta caccttcca 240  
cttgctgaan aagtcanggc ttcttggtg atccatctgc cttingtggt gctgcccngt 300  
tggtgctgc caccacaact gtcctgctg ctgctgcnc ccancctaag ttnaaaccca 360  
agaaaatccg aagatccgan aaagatntgg attgggtctc ttgactaat caccaaaa 418

<210> 332  
<211> 486  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (9)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (49)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (379)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (415)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (446)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (478)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (485)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (486)

<223> n equals a,t,g, or c

<400> 332

```
acgggaccnt gggaccggcg tcgggggtcg cggggaccat gcagcgganc tccctgccct 60
tcgctatcct gacgctggtg aacgccccgt acaagcgagg attttactgc ggggatgact 120
ccatccggta cccctaccgt ccagatacca tcacccacgg gctcatggct ggggtcacca 180
tcacggccac cgtcatcctt gtctcggccg gggaaacctt cctgggtgtac acagaccggc 240
tctattctcg ctcggaactt aacaactacg tggctgctgt atacaagggtg ctggggactt 300
cctgtttggg gctgccgtga gccagtctct gacagacctg gccaaagtaca tgattggggc 360
tctgaagccc aattctaanc gtctgcgaac ccgattgaac cggatcaatgc tcgtnatgtg 420
cagtggagaa gtttgcaggg aacctnttga ttcacgagca gtgtttttaa tcggaatntc 480
tttgann
```

486

<210> 333

<211> 268

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (36)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (69)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (78)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (87)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (105)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (108)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (160)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (218)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (244)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (260)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (263)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (264)  
<223> n equals a,t,g, or c

<400> 333  
cccacgctgt ccgatgattt gtcacaatct tatcantaat cattactctg ttttttatat 60  
ttcaactana agtatcanaa tatagcnttc cagaaaaccc cgaancanag tcaactgacta 120  
catcaaagtc tactacacct tgagaaaaca aatgaacgan aatctatttt cctcattcat 180  
taccccaaca ataataggac tccctatcgt aattattntc actatgtttc caagcattga 240  
tatncccatc acctacccgn ctntcaa 268

<210> 334  
<211> 517  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (214)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (259)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (302)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (332)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (360)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (410)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (436)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (447)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (463)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (489)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (496)

<223> n equals a,t,g, or c

<400> 334

```
cggaaggag cgcctactaa ggacgccgtc gaggtccggg ggcctcaac tctatagctc 60
taactggcta gaagtgccca acgtggaatg tttctttttt aaaggcggct cttgaagcga 120
cccgggaagcg gaagtgggaag aaagtctctag tggcttgaga ttaagcctga tcaagatgac 180
aacctcccaa aagcaccgag acttcgtggc agancccatg ggggagaacc agtggggaac 240
ctggctggga ttggtgaant cctgggcaag aaactggaag aaagggtttt gacaaggcta 300
tnttgtcttg gccatttctg gtgctaaaaa anataaaaaac tctcccggaa tggtgaaaaan 360
ctttttgggc caccacaacat cccgaatgtc cgatgctcca aaatgtgcan cctcttttat 420
gtctttggaa tctctncccc ccccccattt tgaccaattg gancccccctt cctcaagaaa 480
atgtttgttnc ccccanttcc ggttttgatt tccccac 517
```

<210> 335

<211> 297

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (19)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (155)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (156)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (164)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (166)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (167)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (171)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (201)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (224)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (226)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (244)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (245)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (246)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (252)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (265)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (267)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (286)  
<223> n equals a,t,g, or c

<400> 335  
ctccgcgcaaat tgaaccctnc actcaaaggg aaacaaaagc tggagctcca ccgcgggtgac 60  
ggccgctcta gaactagtgg ggggcccggt acccaattcg ccctatagtg agtcgtatta 120  
caattcactg gccgtcgttt tacaacgtcg tgacnnggaa aacntnnaat ncttccggct 180  
cgtatgttgt gtggaattgt nagecgataa caattcacac aggnancagc tataaccatg 240  
attnnnccaa gntcgaaatt aacntnact aaaggggaca aaagtngggg ctccacg 297

<210> 336  
<211> 386  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (50)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (128)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (148)



<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (185)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (187)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (200)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (204)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (244)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (251)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (261)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (265)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (272)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (275)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (286)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (302)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (304)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (314)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (315)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (322)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (328)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (337)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (344)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (346)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (359)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (363)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (365)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (380)  
<223> n equals a,t,g, or c

<400> 336  
gatgggcagc gactacatcc gtgaggtgaa tgtggtgaag tctgcccgtg tcggttattc 60  
caaaatgctg ctgggtgttt atgcctactt tatagagcat aagcagcgca acacccttat 120  
ctggttgncg acggatggtg atgcccnga actttatgaa aaaccacgt tgagcccgac 180  
tattngngat attccgtcgn tgcntggggc tggcccgtg gtatggcaaa aaagcaccgg 240  
gttnaacaag ntcaaccatg naagngttcc anctnaatgg gggggncccc gtaaccaaat 300  
tngncctata agtnnatggg antttaanaa ttcaatnggc cctngntttt aaatggtgng 360  
tgntnggcct tttttttttn gtttgt 386

<210> 337  
<211> 506  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (13)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (307)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (340)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (360)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (404)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (412)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (414)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (437)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (439)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (469)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (470)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (471)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (472)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (481)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (483)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (501)

<223> n equals a,t,g, or c

<400> 337

```

aattcggcag agnattgaca tcaggaagga cctctatgct aacaatgtcc tatcaggggg 60
caccactatg taccttgga ttgccgaccg aatgcagaag gagatcacgg ccctagcacc 120
cagcaccatg aagatcaaga tcattgcccc tccggaggcg caaatactct gtctggatcg 180
gtggctccat cctggcctct ctgtccacct tccagcagat gtggatcagc aaacagggaa 240
tacgggtgaag ccgggccttc cattgtccac cgcaaagtct ttcttaaaac acttttcctg 300
gttcctnttc tgtcttttag gcacacaact gtggaatgtn cctgtgggaa tttatggccn 360
tttcagtttc tttttccaaa tcattcctag ggccaaagtt ttgnattggt tnanccatgg 420
ggttttttta aataaantnt ggaaataggg ttaattgggt aaaaaaaann nnaaaaaaaa 480
ntntgggggg ggggggcccg ntaccc 506

```

<210> 338

<211> 623

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (441)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (508)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (509)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (513)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (537)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (565)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (597)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (599)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (612)

<223> n equals a,t,g, or c

<400> 338

```
gcggaacttg ctactaccag caccatgccc taccaatatc cagcactgac cccggagcag 60
aagaaggagc tgtctgacat cgctcaccgc atcgtggcac ctggcaaggc catcctggct 120
gcagatgagt ccaactgggag cattgccaaag cggctgcagt ccattggcac cgagaacacc 180
gaggagaacc ggcgcttcta ccgccagctg ctgctgacag ctgacgaccg cgtgaacccc 240
tgcattgggg gtgtcatcct ctccatgag acaactctacc agaaggcgga tgatgggcgt 300
cccttccccc aagttatcaa atccaagggc ggtgttgttg gcatcaaggc agacaagggc 360
gtggtccccc tggcagggac aaatggcgag actaccaccc aagggttgga tgggctgtct 420
gagcgctgtg ccaggtacaa ngaaggacgg agctgacttc ggccaagtgg cgttgtgtgc 480
ttaagaatgg gggaacacac cccctcannc ctnggcata tggaatatgc caattgntct 540
ggccccgtat gccagtatct ggcancagaa tgcattgggc cattcgggga gtctgananc 600
tcctgatggg ancatgactt gaa 623
```

<210> 339

<211> 344

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (88)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (157)

<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (171)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (210)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (298)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (317)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (330)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (343)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (344)  
<223> n equals a,t,g, or c

<400> 339  
tcgacccacg cgtccgcttc aacatgattt gtcacaatct tatcaataat cattactctg 60  
ttttttatat ttcaactaaa agtatcanaa tatagctttc cagaaaaccc cgaaccaaag 120  
tcactgacta catcaaagtc tactacacct tggaganaac aaatgaacga naatctattt 180  
tcctcattca ttacccaac aataataggn ctocctatcg taattattat cactatgttt 240  
ccaagcatta tattcccatc acctaccga ctaatcaata atcgactcat ctccattnca 300  
acaatggatt agtgcantga acatgcaaan gcaaggatta tcnn 344

<210> 340  
<211> 345  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (6)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (13)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (31)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (88)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (90)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (128)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (135)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (138)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (146)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (153)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (172)  
<223> n equals a,t,g, or c



<220>  
<221> misc feature  
<222> (173)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (296)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (313)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (339)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (343)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (345)  
<223> n equals a,t,g, or c

<400> 340  
agacangctc tantacgact cactataggg naaagctggt acgcctgcag gtaccggtcc 60  
ggaattcccg ggtcgaccca cgcgtccngn aggaggggac agctgcgggc gcggggaggg 120  
ggcgccgngc cgcgnggngc catggnggac agnagagccg ggagtcgag annccggccc 180  
gcagcccagag atgtcgccgc catggcttcg ccgcagctct gccgcgcgct ggtgtcggcg 240  
caatgggtgg cggaagcgct gcgggccccg cgcgctgggg cagcctctgc agctgntagg 300  
acgcctcctg gtnacctggc cggaagctgg ggggcgcgna cgncn 345

<210> 341  
<211> 170  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (20)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (23)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (43)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (86)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (160)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (163)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (164)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (170)

<223> n equals a,t,g, or c

<400> 341

```
accacgcgt cgcacacgn tcncgactag ttctagatcg cgnacggccg ctctagagga 60
tccaagctta cttggacatg catgcnacgt catagctctt ctatagtgtc acctaaattc 120
aattcactgg ccgtcgtttt acaacgtcgt gactgggaan atnntaaaaan 170
```

<210> 342

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (238)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (273)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (328)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (337)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (351)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (366)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (384)  
<223> n equals a,t,g, or c

<400> 342  
aatgacttgg ttgagtactc accagtcaca gaaaagcattc ttacggatgg catgacagta 60  
agagaattat gcagtgtctgc cataaccatg agtgataaca ctgcggccaa cttacttctg 120  
acaacgatcg gaggaccgaa ggagctaacc gcttttttgc acaacatggg ggatcatgta 180  
actgccttgg atcgttggga accggagctg aatgaagcca taccaaacga cgagcgtnac 240  
accacgatgc ctgtagcaat ggcaacaacg ttngcaaact attaaactggc ggactactta 300  
ctctagcttc ccggcaacaa tttatagnct tggtggnnggc gggtaaagtt ncaaggccca 360  
tttttngggt tggccttcgc gttngtt 387

<210> 343  
<211> 186  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (26)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (64)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (71)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (109)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (152)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (153)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (160)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (183)  
<223> n equals a,t,g, or c

<400> 343  
gctgcaggaa attaacagag tctacnagga aatgtacaag actgatctgg agaaagacat 60  
tatntcggac ncatctggtg acttccgcaa gctgatgggt gccctggcna aagggttaaaa 120  
aacagaagaa tgggtccgtcc ttgaatatga anngaatan ccacatgccc ggatttcctt 180  
ganccc 186

<210> 344  
<211> 611  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (8)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (11)  
<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (285)

<223> n equals a,t,g, or c

<400> 344

```
tgcaaggnga nactaccctc actaaaggga acaaaagctg gagctccacc gcggtgcggc 60
cgctctagaa ctagtggatc ccccgggctg caggaattcg gcacgagctg cgttgggctc 120
cggaagccg ttcgggctgg ggctgtcggc cgcggggcgg aggcactcgc gcgggggatg 180
gcccactgcg tgaccttggt tcagctgtcc atttctgtg accatctcat tgacaaggac 240
atcggtcca agtctgacct actctgcgtc cttttacagg atgtnggagg gggcagctgg 300
gctgagcttg gccggactga acgggtgcgg aactgctcaa gccctgagtt ctccaagact 360
ctacagcttg agtaccgctt tgagacagtc cagaagctac gctttggaat ctatgacata 420
gacaacaaga cgccagagct gagggatgat gacttcctag ggggtgctga gtgtcccta 480
ggacagattg tgtccagcca ggtactgact ctccccttga tgctgaagct ggaaaacctg 540
ctgggcgggg gaccatcacg gtctcagctc aggaattaaa ggacaatcgt gtagtaacca 600
tgaggtaga g 611
```

<210> 345

<211> 344

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (289)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (296)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (329)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (331)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (342)

<223> n equals a,t,g, or c

<400> 345

```
tttcttcta cagtattcct gaatttgacg aatggaaaaa acatatagaa aaccagaaaag 60
cctggaaaat aaagtactat aaaggattgg gtactagtac agctaaagaa gcaaagggaat 120
atthtgcgtga tatggaaagg catcgcatct tgtttagata tgctgggtcct gaagatgatg 180
```

```
ctgccattac cttggcattt agtaagaaga agattgatga cagaaaagaa tggttaacaa 240
atatttatgga agaccggaga cagcgtagct acatggctta ccagaggant gattcnctct 300
caactcagac atgaaagatc tataccacnc ntgttgatgg cntt 344
```

<210> 346

<211> 506

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (392)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (452)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (453)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (472)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (480)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (495)

<223> n equals a,t,g, or c

<400> 346

```
ggaaaagccc aaggaaaaag caaagaatag caaaaaaaag ggggccaaga aggaagtgg 60
tggttgatgg cttctttttt cttcagttag ttttttcccc aacagggtct gatggtcctt 120
tggctaccag caaaccagtc cctgcagaaa agtcagggtct tccagtgggt cctgagaacg 180
gagtagaact ttccaaagag gagctgatcc gcaggaagcg cgaggagtcc attcagaagc 240
atgggagggg tatggagaag tccaacaagt ccacgaagtc agatgctcca aaggagaagg 300
gcaaaaaagc accccgggtg tgggaactgg gtggctgtgc taacaaagaa atgttgatt 360
acagtacttc caccaccaat ggaaccctg angttgctt tgtctgagga cattaacctt 420
gattccaagg gactgggtct ggggggcaact tnnngatctg gactgcacac tntgatgacn 480
aagggttgtg taaantttcc aaacta 506
```

<210> 347

289

<211> 444  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (289)  
<223> n equals a,t,g, or c

<400> 347  
cggaagggag accatgttcc gagcggcggc tccggggcag ctccggcggg cggcctcatt 60  
gctacgattt cagagtaccc tggtaatagc tgagcatgca aatgattccc tagcacccat 120  
tactttaaat accattactg cagccacacg ccttggaggt gaagtgtcct gcttagtagc 180  
tggaacaaaa tgtgacaagg tggcacaaga tctctgtaaa gtagcaggca tagcaaaaagt 240  
tctggtggct cagcatgatg tgtacaaagg cctacttcca gaggaactna caccattgat 300  
tttggcaact cagaagcagt tcaattacac acacatctgt gctggagcat ctgccttcgg 360  
aaagaacctt ttgcccagag tagcagccaa acttgagggt gccccgattt ctgacatcat 420  
tgcaatcaag tcacctgaca catt 444

<210> 348  
<211> 358  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (19)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (52)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (187)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (280)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (295)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (301)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (317)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (348)  
<223> n equals a,t,g, or c

<400> 348  
ggcagagaag cagaagcgnc tcagttagag tccagcaaaa ggtttgccaa anagtttatg 60  
gacagacatg gaatcccaac cgcacaatgg gaaggctttc accaaacctg aaaggaagcc 120  
tgcagcttca ttttgagtgc agacttcctt gctttggttg tgaaaggcca gtggtcttgc 180  
agctggnaaa aggggtgatt gttgcaaaga gcaaagaaga ggcttgcaag ctgtacaaga 240  
gatcatgcag gtaggctggg tcttctggaa aaatttactn ttgtattcat actgnatgaa 300  
ntaccgtttt aagtttnaaa aatgttcctc acattaaggg aaattctntt ttgcaacc 358

<210> 349  
<211> 321  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (187)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (206)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (240)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (294)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (295)  
<223> n equals a,t,g, or c



<220>  
<221> misc feature  
<222> (301)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (316)  
<223> n equals a,t,g, or c

<400> 349  
ggcgctttgc tctgtccacc aagattcctg acaccaaagg ctgcttgacg tgtcgtgtgg 60  
tgcggaaccc ctacacgggt gccaccttcc tgctggccgc cctgcccacc agcctgctcc 120  
tgctgcagtg gtatgagccg ctgcagaagt ttctgctgct gaagaacttc tccagccctc 180  
tgcccanccc agctgggatg ctgganccgc tgggtgctgga tgggaaggag ctgccgcagn 240  
gttttttttg ggccgaaggg cctaaagggc ccggttgccg gttcctgttc caanncctgc 300  
ncctgggagg ttggcnttaa g 321

<210> 350  
<211> 742  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (618)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (653)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (658)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (683)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (689)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (702)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (707)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (714)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (719)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (722)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (734)

<223> n equals a,t,g, or c

<400> 350

```
ggtcacgctg acccagtgtc cggaaaagct ggtgcagctc atcctgcacg aatacaagat 60
cttcaatgca gaagtgtctt tccgagaaga ctgctccccg gacgagttca tcgatgtgat 120
cgtgggcaac cgggtgtaca tgccctgcct gtatgtttat aacaaaatcg accagatctc 180
catggaagag gtggaccgcc tggcccgaac acccaacagt gtggtcatca gctgcggcat 240
gaagctgaac ctggactatc tgctggagat gctctgggag tacttgcccc tgacctgcat 300
ctacaccaag aagagaggac agaggccaga cttcacagac gccatcattc tccggaagg 360
ggcctcagtg gagcacgtgg gcaccagcac caagtacagt ccgcagcggg tgggcctgac 420
ccacaccatg gagcatgagg acgtcatcca gatcgtgaag aagtaacggc gcctgccggg 480
ccttccgccc acctgtctgt ctcccttggg aggtggtccc actgggacac acaaacaccc 540
aaacagaaaa atacaaatac acgtacccca agaaggggtc cctcaagtct ctgctattta 600
cagaagtttc ttcagtangc agacaaaaa tgtgttgggc aaaagggctc ggntggangc 660
atttccata agactgagcc ctnttcattg ggggttttga gnttgantgc ttancctgna 720
tntgtgcctc caanccctg ac 742
```

<210> 351

<211> 272

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (167)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (251)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (272)

<223> n equals a,t,g, or c

<400> 351

```
aatcaggcgg gactgacggc agatcgtatg ctggtcctgt ccagagccgg gcaggcggca 60
gggctgacgt ttaaccagac cagcgagtca ctcagcgcac tggttaaggc gggggtaagc 120
ggtagaggctc agattgcgtc catcagccag agtgtggcgc gtttctnctc tgcattccggc 180
gtggaggtgg acaaggctcg tgaagccttc gagggggggc cgtacccatt tgcctatagt 240
aagcgtatta naataattgc cgtgttttaa an 272
```

<210> 352

<211> 256

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (170)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (236)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (248)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (251)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (252)

<223> n equals a,t,g, or c

<400> 352

```
gcagacgtcc agagcagagt cagccagcat gaccgagcgc cgcgtcccct tctcgtcct 60
gcggggcccc agctgggacc ccttcgcga ctggtaccgc catagccgcc tcttcgacca 120
```

```
ggccttcggg ctgccccggc tgccggagga gtggtcgag tggtaggcn gcagcagctg 180
gccaggctac gtgcgcccc tgccccccgc cgcacgaga gcccgcagt ggccgngccc 240
gctacagncg nncgct 256
```

```
<210> 353
<211> 592
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc feature
<222> (35)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (54)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (93)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (277)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (480)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (485)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (522)
<223> n equals a,t,g, or c
```

```
<220>
<221> misc feature
<222> (545)
<223> n equals a,t,g, or c
```

```
<400> 353
ggttccttc cacgctgttg aagcattgta ctttnggtct tcatgataaa tctngctgct 60
```

295

```

gctcactcgt tgggtccgtg ccacctttaa aanctgtaac actcaccgag aaggtctgca 120
acttcactcc tggggccagc aagaccacga gtgcaccgag aggaatgaac aactctggac 180
acaccatctt taagaaccgt aatactcacc gcaagggtct gcaacttcat tcttgaagtc 240
agtgaggcca agaaccatc aattccgtac acatttnggt gactttgaag agactgtcac 300
ctatcaccaa gtggtgagac tattgccaag cagtgaact attgccaagt ggtgagacca 360
tcaccaagcg gtgagactat cacctatcgc caagtgtcc taagtgtgaa cgtgaagtcc 420
ccagccctgc tgctgagcca gttgctgccc tacatggaga acaagaaggg tgctgtcatn 480
ctggnetctt ccattgcagc ttataatcca gtagtggcgc tnggtgtcta caatgtcagc 540
aaganagagc tgctggggtc tcactagaac actggcattg ggcttggccc cc 592

```

&lt;210&gt; 354

&lt;211&gt; 539

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (4)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (223)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (225)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 354

```

cacnaacct cactaaaggg aacaaaagct ggagctccac cgcggtgacg gccgctctag 60
aactagtgga tcccccgggc tgcaggaatt cggcacgagt cgtctcaggc tcgtagttcg 120
ccttcaacat gccggaacca gcgaagtccg ctcccgcgcc caagaagggc tcgaagaaag 180
ccgtgactaa ggcgcagaag aaggacggca agaagcgcaa ggnanccgca aggagagcta 240
ctccgtatac gtgtacaagg tgctgaagca ggtccacccc gacaccggca tctcctctaa 300
ggccatggga atcatgaact ccttcgtcaa cgacatcttc gaacgcatcg cgggtgaggc 360
ttcccgctg gcgcattaca acaagcgctc gaccatcacc tccagggaga tccagacggc 420
cgtgcgcctg ctgctgcccg gggagttggc caagcacgcc gtgtccgagg gcaccaaggc 480
cgtcaccaag tacaccagcg ctaagtaaac ttgccaagga gggactttct ctggaattt 539

```

&lt;210&gt; 355

&lt;211&gt; 435

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (296)

&lt;223&gt; n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (299)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (396)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (419)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (421)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (422)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (424)  
 <223> n equals a,t,g, or c

<400> 355  
 gcttcgctca cctgccaag agtacctttg tggttgatga atttaagcgc aagtactcca 60  
 atgaggacac actctctgtg gcactgccat atttctggga gcactttgat aaggacggct 120  
 ggtccctgtg gtactcagag tatcgcttcc ctgaagaact cactcagacc ttcagagct 180  
 gcaatctcat cactggaatg ttccagcgac tggacaagct gaggaagaat gccttcgcca 240  
 gtgtcatcct ttttggaaac aacaatagca gctccatttc tggagtctgg gtcttnccng 300  
 gccaggagct tgcctttccg ctgagtccag attggcaagt ggactacgaa gtcatacaca 360  
 tggcggaac tggatctggc aagcgaggag acccanacgc tggttcgaga gtacttttnc 420  
 nngngagggg gcctt 435

<210> 356  
 <211> 502  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (21)  
 <223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (168)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (239)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (243)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (252)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (275)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (288)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (292)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (298)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (316)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (317)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (324)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (328)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (339)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (348)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (364)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (372)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (386)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (390)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (393)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (397)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (403)



<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (413)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (417)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (419)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (420)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (425)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (426)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (430)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (437)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (440)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (442)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (445)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (449)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (452)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (457)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (458)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (459)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (461)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (476)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (478)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (485)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (497)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (499)  
<223> n equals a,t,g, or c

<400> 356  
aattcggcac gagagggagt ntgagcaagg ggtgtacacc tgcacagcac agggcatttg 60  
gaagaatgaa cagaagggag agaagattcc tcggtgcttg ccagtttggt ggaagcccgt 120  
gaaccccgtg gaacagaggc agcgcatcat cggagggcaa aaagccangg ggatagtggg 180  
ggcgtttttg cagtaaggga cccgaacact gatcgctggg tggccacggg catcgtgtnc 240  
ctngggcatc gngtgcagca gggccttatg gcttnttaca ccaaagtnc cnaacttncg 300  
tggccttgga tcaagnnaga cctngganca ggaggactnc cgccccanca ttcactaggt 360  
tccnaatcca gngagcagtt tcgcanaaan canccanaca cancttcccc ctntttngnn 420  
accnncagn gtctctnttn anancctnc tngcacnnna ncccacaacc ccccnncnc 480  
cccnccccc ccccnncnc cc 502

<210> 357  
<211> 440  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (45)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (236)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (262)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (293)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (300)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (316)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (339)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (360)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (362)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (378)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (387)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (389)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (402)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (407)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (418)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (426)  
<223> n equals a,t,g, or c

<400> 357  
aatatatcga acagtcaggt taacaggctg cggcattttg tccgngccgg gcttcgctca 60  
ctgttcaggc cggagccaca gaccgccgtt gaatgggagg atgctaatta ctatctcccg 120  
aaagaatccg cataccagga agggcgctgg gaaacactgc cctttcagcg ggccatcatg 180  
aatgcgaatg ggcagcgact acatccgtga gtggaatgtg gtgaagtttg cccgtntcgg 240  
ttattccaaa atgctgctgg gngtttatgc ctactttata gggcataagc agnggaacan 300  
ccttatttgg tttccncagg atggtggatg cccgagaant ttttgaaaaa cccacgttgn 360  
gncgattatt tcgggganatt ttccgngnt gttgggggtt gncgccntgg gttttggnaa 420  
aaaganccgg gtaaaagggt 440

<210> 358  
<211> 234  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (16)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (46)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (92)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (162)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (166)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (175)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (208)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (230)

<223> n equals a,t,g, or c

<400> 358

```
ggaaagggtg tttatncctc atggactaat tatggacagg actgancgtt ttgctcgaaa 60
tgtgatgaag gagatgggag gccatcacat tntagtcctc tttttgctca aggggggcta 120
taaatttttt gctgacctgc tggattacat caaaggactg antagnaaat agtgnataga 180
tccattcctc atgaactgtg gatttttngc agatctgaag agctattgtg atga      234
```

<210> 359

<211> 668

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (15)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (19)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (20)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (295)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (512)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (552)

<223> n equals a,t,g, or c

<220>

<221> misc feature

305

<222> (558)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (559)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (579)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (588)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (593)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (659)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (667)  
<223> n equals a,t,g, or c

<400> 359  
ctgactccag tttgntatnn ccatgattac gccaaagtct aatacgactc actatagggg 60  
aagctggtac gcctgcaggt accggtccgg aattcccggg tcgaccacg cgtccggggg 120  
gtttgaggtata cataagaaaa atgtaagggg tgaattcact tattatgaaa tacaagataa 180  
tacaggggaag atggaagtgg tgggtgcatgg acgactgacc acaatcaact gtgaggaagg 240  
agataaaactg aaactcacct gctttgaatt ggcaccgaaa agtgggaata ccgngagatt 300  
gagatctgta attcatagtc acatcaaggt catcaagacc aggaaaaaca agaaagacat 360  
actcaatcct gattcaagta tggaaacttc accagacttt ttcttctaaa atctggatgt 420  
cattgacgat aatgtttatg gagataaggt ctaagtgcct aaaaaaatgt acatatacct 480  
ggttgaaata caacactata catacacacc ancatatata ctagcttggt aatcctatgg 540  
aaatggggta tntggagnnc ttttttaatt tttcatagnt tttttttnat aanaatggca 600  
tattttggat ctacaacttc tatgatttga aaaaatacct taacccttat cttttttgng 660  
aaaaaana 668

<210> 360  
<211> 401  
<212> DNA  
<213> Homo sapiens

<400> 360  
caccattacc agcggcggca atcctccggc cttttccctg acaccggacg gaaagctgac 60  
cgctaaaaat gcggatatca gtggcagtgt gaatgcgaac tccgggacgc tcagtaatgt 120  
gacgatagct gaaaactgta cgataaacgg tacgctgagg gcggaaaaaa tcgtcgggga 180  
cattgtaaag gcggcgagcg cggcttttcc gcgccagggtg gaaagcagtg tggactggcc 240  
gtcaggtagc cgtactgtca ccgtgaccga tgaccatcct tttgatcgcc agatagtggg 300  
gcttccgctg acgtttcgcg gaagtaagcg tactgtcagc ggccaggacaa cgtattcgat 360  
gtgttatctg aaagtactga tgaacgggtgc ggtgatttat g 401

<210> 361  
<211> 273  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (156)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (189)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (236)  
<223> n equals a,t,g, or c

<400> 361  
accggaacac ggcactggtc ggcgtgcagg tggactcgga gcagttcggc agccagcagg 60  
tgagccgtaa ttatcatctg cgcgggcgta ttctgcagggt gccgtcgaac tataacccgc 120  
agacgcggca atacagcggg atctgggacg gaacgnntaa accggcatac agcaacaaca 180  
tggcctggng tctgtgggat atgctgaccc atccgcgcta cggcatgggg aaacgncttg 240  
gtgcggcgga tgtggataaa tgggcgctgt atg 273

<210> 362  
<211> 248  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (5)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (37)  
<223> n equals a,t,g, or c



<220>  
<221> misc feature  
<222> (41)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (52)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (74)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (145)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (161)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (185)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (194)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (210)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (218)  
<223> n equals a,t,g, or c

<400> 362  
cgctcngtcgg gcgagcgatg atgcggaagg ttacctngat nttttcaaag gnaagataac 60  
cgaatcccat ctncgcaagg agctgctgga aaaagtcgag ctgacggagg ataacgccag 120  
cagactggag gagttttcga aagantggaa ggatgccagt nataagtgga atgccatgtg 180  
ggctntcaaa attnagcaga ccaaagacgn caaacgantt ttattctgct atttagtagt 240

aagatcag

248

&lt;210&gt; 363

&lt;211&gt; 149

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (131)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (137)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (144)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (145)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (147)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 363

tgccggactt tcacgtgag gatgactggt ggcgtaacgg ccagaatctc tatctggata 60

atctggaggc gacggggctg taccaggtgc cgttgctcagc ggcacagccg ggcgatgtgc 120

tgctgtgctg ntttgntca tcannngc 149

&lt;210&gt; 364

&lt;211&gt; 352

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (4)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (93)

&lt;223&gt; n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (196)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (319)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (322)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (325)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (338)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (340)  
<223> n equals a,t,g, or c

<400> 364  
gcanaaagaa aatggcacag taacagctgc caatgccagt acactgaatg atggagcagc 60  
tgctctggtt ctcattgacg cagatgcagc gangaggctc aatgttacac cactggcaag 120  
aatagtagca ttgtctgacg ctgctgtaga acctattgat ttccaattg ctctgtata 180  
tgctgcatct atggtnccta aagatgtggg attgaaaaaa gaagatattg caatgtggga 240  
agtaaattgga agcctttagt ctggtgtgac tagcaaacat taaaaatgtt ggagattgga 300  
tccccaaaaa gtgaatatnc anggnaggag ctgtttcncn ggggacatcc ca 352

<210> 365  
<211> 272  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (37)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (42)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (44)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (47)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (80)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (91)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (116)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (132)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (145)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (190)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (226)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (242)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (260)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (261)

<223> n equals a,t,g, or c

<400> 365

```
aggaaaaagc cgggcctcct ggtggggcag tgccggncac ancntgntgc cctgcagagg 60
ggcttggtgcc gctgctggan tgacagcctt ncgaggcttt gctgtctcgg cacggnagggt 120
ctggcaaacc anggacagac caggnacatg ggaccaaagc cggaacctcc tgctcaacgg 180
gaagtcctan cccaccaaag tgcgcctgat ctgggggggc tccctncccc cagtcaagcg 240
gncggcggat gaactggatn nacgccccgg at 272
```

<210> 366

<211> 254

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (23)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (192)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (208)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (209)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (236)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (244)

<223> n equals a,t,g, or c

<400> 366

```
ggctctacta ggactcacta tanggaaagc tggtagcct gcaggtagcg gtccggaatt 60
cccggtcgga cccacgcgtc cgcttctctg cctagaaggg ataatattat cactcttcgt 120
tataataaca atcaccatct taattaacca ccttacatta gccagcataa cccctatcat 180
ccttcttgta tntgcagcct gtgaagcnc actggggctt atccctttta gttatnatct 240
caantacata cgga 254
```

<210> 367

<211> 185

<212> DNA

<213> Homo sapiens

<400> 367

```
gattggattc gacaacaaaa aagacctgct tatctcggtg ggcgatttgg ttgatcgtgg 60
tgcagagaac gttgaatgcc tggaattaat cacattcccc tggttcagag ctgtacgtgg 120
aaacctgag caaatgatga ttgatggctt atcagagcgt ggaaacgtta atcactggct 180
gctta 185
```

<210> 368

<211> 458

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (15)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (27)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (170)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (193)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (232)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (246)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (250)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (316)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (340)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (395)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (399)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (404)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (415)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (433)  
<223> n equals a,t,g, or c

<400> 368  
agnnccnatag aaagnacgcc tgcagggnacc ggtccggaat tcccgggtcg acccacgcgt 60  
ccggagttag ccttgaacgc ctggacctgg acctcacagc tgacagccag ccacccgtct 120  
tcaaggtctt cccaggcagt accactgagg actacaacct tattgttatn gaacgtggcg 180  
ctgccgctgc acnaccggcc agccagggac tgcgcctgca ggaacccctg gngccccacc 240  
cctggntggn atggccattg tcaaggagga ggagacggag gctgccattg gagccctcc 300  
tactgccact gagggncctg agaccaaacc tgtgttatn gctcttgagg agggctctgg 360  
tgctgagggt tcccggctgg actcactagt ggcanaacna ctcnnggctgg aagtngtagc 420  
tctgaggggac tcngcccagc tggtggccgg gacctgat 458

<210> 369  
<211> 288  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (15)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (17)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (47)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (56)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (71)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature



315

<222> (103)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (114)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (225)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (239)  
<223> n equals a,t,g, or c

<400> 369  
gcgctggagc tgctngngca ctgcggcgtg tgcagagagc gcctgcnacc cgaganggag 60  
ccccgcctgc ngccctgttt gcactcggcc tgtagtgcc tgcntagggcc cgcngccccg 120  
ccgccgccaa cagctcgggg gacggcgggg cggcgggga cggcaccgtg gtggactgtc 180  
ccgtgtgcaa gcaacagtgc ttctccaaag acatcgtgga gaatnatttc atgcgtgana 240  
gtggcagcaa ggctgccacc gacgcccagg atgcgaacca gtgctgca 288

<210> 370  
<211> 292  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (47)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (53)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (60)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (61)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (101)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (141)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (263)  
<223> n equals a,t,g, or c

<400> 370  
ccatctttgc attgttctc atccgcctcc ttgctcgccg cagccgntc cgcgcgcgn 60  
ntcctccgcc gccgcggact ccggcagctt tatcgccaga ntccctgaac tctcgctttc 120  
tttttaatcc cctgcatcgg ntcaccggcg tgccccacca tgtcagacgc agccgtagac 180  
accagctccg aaatcaccac caaggactta aaggagaaga aggaagtttt ggaaagaggc 240  
agaaaatgga agagacggcc ctnccttaacg gggaatgcta atttagggaa at 292

<210> 371  
<211> 477  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (35)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (276)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (313)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (342)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (374)  
<223> n equals a,t,g, or c

317

<220>  
<221> misc feature  
<222> (399)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (410)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (427)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (434)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (447)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (448)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (451)  
<223> n equals a,t,g, or c

<400> 371  
ggcacaggat aattttaagc atttaaatgg aattnatctt ttctactgta ttgatccaaa 60  
tggttccaag cataaaagaa cggacagatc aattttatgt tgtttacgaa aaggagaatc 120  
tggccagtca tggcaagggt taacaaaaga aaggggcaaag cttaattggc ttagtgctga 180  
cttcaataat tgggaaagac tgggaagatg attcaaatga agacatgtct aattttgaat 240  
cgtttctctg aggattcaca agacagtgat gatggnaaaa atgccagatc tgggagtaag 300  
ggaatattgt ccntcacctg ggtttttgag gaaaggaaaa tnaactttct ctggcaagggt 360  
tttcataat ttngaggaa ttccccgagt ttgtagcnc ctaaagggn gttatgctcg 420  
tatttgnccc actntaaccc ctttttnnca nccggtttgt ttttttaaaa gggcttc 477

<210> 372  
<211> 443  
<212> DNA  
<213> Homo sapiens

<220>

<221> misc feature  
<222> (14)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (67)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (74)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (107)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (116)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (123)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (171)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (174)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (220)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (222)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (293)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (314)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (329)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (335)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (340)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (351)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (364)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (373)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (407)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (411)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (426)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (430)

<223> n equals a,t,g, or c

<400> 372

```
ggcagagcac tgtnaaacta gaacatgcta aatctgttgc ttccagagcc actgtcctcc 60
agaaganatc cttnaccctt gtaggaatgt ttttgaaact aaatttnatg aacgtnaaat 120
ttncagtggt ttattatgaa cttccttgtc gaagttgaaa ggtgaacaac nctnatattg 180
caaataccgt agagcttcag agtgcaagat tctccactgn angttgggca ttcacaaatg 240
ttggatcttt cccaccgtgg gatgaagggg tcagaggcat tgcacccaaa atnaccggg 300
tgaacatacc cagnccaaag cccaggggna cattnatcgn ggacaggccc nccagaattt 360
ggcntgttct ttncagttg gtaggtgtgg aacttggggg tgaattnatt ncttaaccga 420
attttnccgn ttccttaacc gag 443
```

<210> 373

<211> 464

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (20)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (235)

<223> n equals a,t,g, or c

<400> 373

```
cggatccgca ggcgcacgtn gcgatgttgt cctctacagc catgtattcg gctcctggca 60
gagacttggg gatggaaccg cacagagccg cgggcccttt gcagctgcga ttttcgccct 120
acgttttcaa cggaggtact atactggcaa ttgctggaga agattttgca attgttgctt 180
ctgatactcg attgagtga gggttttcaa ttcatacgcg ggatagcccc aaatnttaca 240
aattaacaga caaaacagtc attggatgca gcggttttca tggagactgt cttacgctga 300
caaagattat tgaagcaaga ctaaagatgt ataagcattc caataataag gccatgacta 360
cgggggcaat tgctgcaatg ctgtctacaa tcctgtattc aaggcgcttc tttccatact 420
atgttttcaa catcatcggg ggaacttgatg aagaaggaaa gggg 464
```

<210> 374

<211> 369

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (216)

<223> n equals a,t,g, or c

321

<220>  
<221> misc feature  
<222> (218)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (219)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (221)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (332)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (357)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (360)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (363)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (369)  
<223> n equals a,t,g, or c

<400> 374  
ggcacagcct ctacagccat gtattcggt cctggcagag acttggggat ggaaccgcac 60  
agagccgcgg gccctttgca gctgcgattt tcgccctacg ttttcaacgg aggtactata 120  
ctggcaattg ctggagaaga ttttgcaatt gttgcttctg atactcgatt gagtgaagg 180  
ttttcaattc atacgcggga tagcccaaa tgttgncna ntaacagaca aaacagtcac 240  
tggatgcagc ggttttcatg gagactgtct tacgctgaca aagattattg aagcaagact 300  
aaagatgtat aagcattcca ataataaggc cntgactacg gggggcaatg ctggcangcn 360  
gtntacan 369

<210> 375

322

<211> 313  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (32)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (249)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (259)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (268)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (293)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (308)  
 <223> n equals a,t,g, or c

<400> 375  
 tacccttcat cactaaaggc cgcctgtgcg tnttttttta cgggattttt ttatgtcgat 60  
 gtacacaacc gcccaactgc tggcggcaaa tgagcagaaa tttaagtttg atccgctgtt 120  
 tctgctctc tttttcgtg agagctatcc cttcaccacg gaggaaagtc tatctctcac 180  
 aaattccggg actggtaaac atggcgctgt acgtttcgcc gattgtttcc ggtgaagggt 240  
 atcccgttnc cctggcggnr tccacctntg aatttaaggc cgggataatg tcnaagcccc 300  
 aagcatgnaa gtg 313

<210> 376  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 376  
 cgggttccgg tgaccacgaa ggcggcaaag gcgacggaat ggaggaggtg cctcacgact 60  
 gtccaggggc cgacagcgcc caggcgggca gaggggcttc atgtcaggga tgccccaacc 120  
 agcggctgtg cgcttctgga gcgggggcca ctccggacac ggctatagag gaaatcaaag 180



```
agaaaatgaa gactgtaaaa cacaaaatct tggattgtc tgggaaaggc ggtgttggga 240
aaagcacatt cagcgccac cttgcccac gcctagcaga ggatgaaaac acacagattg 300
ctcttctaga catcgatata tgtgggccat cgattcccaa gataatggga ttggaaggag 360
agcaggttca ccaga 375
```

<210> 377

<211> 434

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (9)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (17)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (22)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (32)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (33)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (47)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (58)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (64)

<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (69)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (73)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (98)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (112)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (116)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (118)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (146)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (151)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (161)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (163)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (193)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (212)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (214)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (228)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (235)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (243)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (250)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (262)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (263)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (264)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (265)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (267)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (279)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (301)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (320)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (330)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (337)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (351)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (370)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (381)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (409)

<223> n equals a,t,g, or c

327

&lt;400&gt; 377

```
ggcagcagng tggctcnagg gngtcacctt cnntgttacc accgttnaca ccaaaagncg 60
gacngagana gtncagaagc tgtgcccagg ggggcagntc ccattcctgc tntatngnac 120
tgaagtgcac acagacacca acaagnttgc ngaatttctg nangcagtgc tgtgccctcc 180
caggtacccc aanctggcag ctctgaaccc tnantccaac acagctgngc tgganatatt 240
tgncaaattn tctgcctaca tnnnnanttc aaaccacagna ctcaatgaca atctggagaa 300
nggactcctg aaagccctgn acgttttagn caattantta acatcccccc nctcagaaga 360
agtggatgan accagtgtg nagtgaaggt gtctctcaga agaagttnt ggatagcacg 420
agctcaccct gggg                                     434
```

&lt;210&gt; 378

&lt;211&gt; 506

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (133)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (294)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (367)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (376)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (386)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (389)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (421)

&lt;223&gt; n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (440)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (443)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (472)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (479)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (492)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (493)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (496)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (503)  
<223> n equals a,t,g, or c

<400> 378  
aattttcact ccctcagaa cataacatag taaatggatt gaattatgaa gaatggtttt 60  
tatgcgactt accgcagcaa aaataaaggg aaagataagc gctcaataaa cctgtctgtt 120  
ttccttaatt cnttgctggc tgataatcat cacctgcagg ttggctccaa ttatttgtat 180  
attcataaaa tcgatggaaa aacttttctc tttaacaaaa caaatgacaa gagtctggtt 240  
cagaagataa atcgctctaa agcttcagtt gaagatatta agaacagcct cgtngatgac 300  
ggaatcattg ggattcccat cttttttgtt tggtgaaggc gacaccattg gtttttgcca 360  
gaactgnttt tcgggncggc cacatncgnt ttgacagggt ttttttaatc ggggaaggga 420  
ntgtccttaa ggcgtggggn gcngttcagt tggggccctg ttggggggac cnccaaggng 480  
gtggttatgg cnnngntttc atnggc 506

<210> 379  
<211> 550  
<212> DNA  
<213> Homo sapiens  
  
<220>  
<221> misc feature  
<222> (6)  
<223> n equals a,t,g, or c  
  
<220>  
<221> misc feature  
<222> (9)  
<223> n equals a,t,g, or c

<400> 379  
gacganacna accctcacta aagggaaacaa aagctggagc tccaccgagg tgcggccgct 60  
ctagaactag tggatcccc gggtgcagg aattcggcac gaggccatcc agactgagga 120  
agaccggaa acttaggggc cacgtgagcc acggccacgg ccgcataggc aagcaccgga 180  
agcaccggc cgccggcggg aatgctggtg gtctgcatca ccaccggatc aacttcgaca 240  
aataccacc aggctacttt gggaaagtgt gtatgaagca ttaccactta aagaggaacc 300  
agagcttctg cccaactgtc aaccttgaca aattgtggac ttgggtcagt gaacagacac 360  
gggtgaatgc tgctaaaaac aagactgggg ctgctcccat cattgatgtg gtgcgacgg 420  
gctactataa agttctggga aagggaaagc tcccaaagca gcctgtcatc gtgaaggcca 480  
aattcttcag cagaagagct gaggagaaga ttaagagtgt tggggggggc tgtgtcctgg 540  
tggttgaag 550

<210> 380  
<211> 573  
<212> DNA  
<213> Homo sapiens  
  
<220>  
<221> misc feature  
<222> (4)  
<223> n equals a,t,g, or c  
  
<220>  
<221> misc feature  
<222> (6)  
<223> n equals a,t,g, or c  
  
<220>  
<221> misc feature  
<222> (10)  
<223> n equals a,t,g, or c  
  
<220>  
<221> misc feature  
<222> (160)  
<223> n equals a,t,g, or c

```

<400> 380
aagncnagan agccaaccct cactaaaggg aacaaaagct ggagctccac cgcggtgcgg 60
ccgctctaga actagtggat cccccgggct gcaggaattc ggcacgagcg caaagaagg 120
tggcgagaag aaaaagggcc gttctgccat caacgaaggn taacccgaga atacaccatc 180
aacattcaca agcgcattcca tggagtgggc ttcaagaagc gtgcacctcg ggcactcaaa 240
gagattcgga aatttgccat gaaggagatg ggaactccag atgtgcgcat tgacaccagg 300
ctcaacaaag ctgtctgggc caaaggaata aggaatgtgc cataccgaat ccgtgtgcgg 360
ctgtccagaa aacgtaatga ggatgaagat tcaccaaata agctatatac tttggttacc 420
tatgtacctg ttaccacttt caaaatttct gtgctaaaca gtgttacagt cgccaagagc 480
ccataaaggg agccctcctg gaagtggatg aggccttggg tctcggtctt tcattgcttc 540
ctgagctgca gcagatgcct ttacaaccaa gct 573

```

<210> 381

<211> 531

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (5)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (8)

<223> n equals a,t,g, or c

```

<400> 381
gcagnacnaa ccctcactaa agggaacaaa agctggagct ccaccgcggt gcggccgctc 60
tagaactagt ggatcccccg ggctgcagga attcggcacg aggcggcggt ggcggcttgt 120
gcagcaatgg ccaagatcaa ggctcgagat cttcgcggga agaagaagga ggagctgctg 180
aaacagctgg acgacctgaa ggtggagctg tccagctgc gcgtcgccaa agtgacaggc 240
ggtgcggcct ccaagctctc taagatccga gtcgtccgga aatccattgc ccgtgttctc 300
acagttatta accagactca gaaagaaaac ctcaggaaat tctacaaggg caagaagtac 360
aagcccctgg acctgcggcc taagaagaca cgtgccatgc gccgcgggct caacaagcac 420
gaggagaacc tgaagaccaa gaagcagcag cggaaggagc ggctgtaccc gctgcggaag 480
tacgcggtca aggcctgagg ggcgcatgtt caataaagca cagtggctga g 531

```

<210> 382

<211> 300

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature



<222> (5)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (40)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (43)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (59)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (171)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (172)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (175)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (179)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (184)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (190)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (203)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (271)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (292)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (293)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (300)

<223> n equals a,t,g, or c

<400> 382

ngggngtacc acaaataaa ggcaaagagg aactgctggn cangagtacg ggggtgtggnc 60  
atgaatcctg tggagcatcc ttttggaggt ggcaaccacc agcacatcgg caagccctcc 120  
accatccgca gagatgcccc tgctggccgc aaagtgggtc tcattgctgc nngcnggant 180  
ggangtctcn ggggaaccaa gantgtgcag gagaaagaga actagtgtctg agggcctcaa 240  
taaaagtttgt gtttatgcc aaaaaaaaaa naaaaaaaaa aaaaaaaaaa annaaagagn 300

<210> 383

<211> 475

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (36)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (146)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (363)

<223> n equals a,t,g, or c

<220>

<221> misc feature

333

<222> (367)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (401)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (404)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (415)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (450)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (451)  
<223> n equals a,t,g, or c

<400> 383  
atgacgccgg tgcagcgggg gggcccgggg gcctgngtgg ccctgggatg gggaaccgcg 60  
gtggcttcgc cgaggtttcg gcagtggcat ccggggccgg ggtgcgggcc gtggacgggg 120  
ccggggccga gccgcggac tcgcgnaggc aaggccgagg ataaggagtg gatgcccgtc 180  
accaagttgg gccgcttgg caaggacatg aagatcaagt ccctggagga gatctatctc 240  
ttctccctgc ccattaagga atcagagatc attgattctt cctgggggct ctctcaagga 300  
tgagttttga agatatgcca tgcagaagca gacctgccg gccacgcacc agttcaagca 360  
ttnttgnaac gggattaaat gccactcgtt tggtttaatg nccnagagtg gcacncatcc 420  
tgggcaaaac tggcaaattt caagtccttn naagtatggg gaaaatggaa cccaa 475

<210> 384  
<211> 127  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (5)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (8)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (31)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (62)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (71)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (103)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (124)

<223> n equals a,t,g, or c

<400> 384

caatntgnag accagattcc taaggctgca naggggacag tgggatctat ttaggaccg 60  
angagattaa ncagagacac aggcaattgt atgtcagcag ctngatttaa cccacctaaa 120  
aggngcgg 127

<210> 385

<211> 317

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (30)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (151)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (187)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (203)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (231)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (264)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (308)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (311)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (316)  
<223> n equals a,t,g, or c

<400> 385  
ggcacgaggg atgtgcgacg tgtgcctggn gtagccccga ctcttgtagc gtcggcatct 60  
gagaccagtg agaaacgccc cttcatgtgt gcttaccag gctgcaataa gagatatttt 120  
aagctgtccc acttacagat gcacagcagg naagcacact ggtgagaaac cataccagtg 180  
tgacttnaag gactgtgaac gangttttct cggtcagacc agctcaaaag ncaccaaagg 240  
aggacataca ggtgtgaacc attnccagtg taaaattggt cagcgaaatt ctcccgtcc 300  
gaccaacnga ngaccna 317

<210> 386  
<211> 433  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (295)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (311)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (359)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (385)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (405)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (407)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (427).  
 <223> n equals a,t,g, or c

<400> 386  
 ttccaagc tatttaggtg aactataga aggtagcctg caggttaccg gtccggaaat 60  
 tcccggtcg acccagcgt ccgccgagag ccttagccga cggaaactgg aactggaac 120  
 cgcagcgcc atgagactcc tccccgctt gctgctgctt ctcttactcg tgttcctgc 180  
 cactgtcttg ttccgaggcg gccccagagg ctgttagca gtggcacaag atcttacaga 240  
 ggatgaagaa acagtagaag attccataat tgaggatgaa gatgatgaag ccgangtaga 300  
 agaagatgaa nccacagatt ttgtagaaga taaaggaggaa gaagatgtgt ctggtgaanc 360  
 taaaacttta ccgagtgcag atacnactat actgttttta aaggngnaga tttccgcca 420  
 ataacantgt gaa 433

<210> 387  
 <211> 407  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (315)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (356)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (359)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (373)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (376)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (407)

<223> n equals a,t,g, or c

<400> 387

```

atttgaagca aacaggcagc gcgcgacaat ggcggtcgct cgtgcagctt tggggccatt 60
ggtgacgggt ctgtacgacg tgcaggcttt caagtttggg gacttcgtgc tgaagagcgg 120
gctttcctcc cccatctaca tcgatctgcg gggcatcgtg tctcgaccgc gtcttctgag 180
tcagggttga gatattttat tccaaactgc ccaaaatgca ggcacagtt ttgacaccgt 240
gtgtggagtg ccttatacag ctttgccatt ggctacagtt atctgttcaa ccaatcaa 300
tccaatgctt attanaagga aagaaacaaa ggattatgga actaagcgtc ttgtanaang 360
aatattaatc canganaaac tgtttaatca ttgaaatggt gtccan 407

```

<210> 388

<211> 244

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (215)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (221)

<223> n equals a,t,g, or c

<400> 388

```

ttcgttcatc tatcgatcg ccacactcac aacaatgagt ggcagatata gcctggtggt 60
tcaggcgggc catttttatt gctgtgttgc gctgtaattc ttctatttct gatgctgaat 120
caatgatgtc tgccatcttt cattaatccc tgaactgttg gttaatacgc ttgaggggtga 180
atgccaataa taaaaaagga gcctgtagct ccctnatgat nttgcttttc atgttcacg 240

```

ttcc

244

&lt;210&gt; 389

&lt;211&gt; 239

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (21)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (55)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (64)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (71)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (116)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (128)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (163)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (185)

&lt;223&gt; n equals a,t,g, or c



<220>  
<221> misc feature  
<222> (196)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (202)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (205)  
<223> n equals a,t,g, or c

<400> 389  
nggactggcg tcagacgtcg nattccggcg cccacggtcg gcttaaacc tggtncaatc 60  
ctgncgcccg ncgtgatgcc agggaagaca gggcgacctg gaagtccaac tacttnctta 120  
agatcatnca acgtattggg atgattatcc taaaatgggt tcnattgggt ggtagcgagt 180  
acganatggt ggggcntcct anagntagta tggcgagcta ggtcccggc taatgttcc 239

<210> 390  
<211> 382  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (5)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (54)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (69)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (102)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (103)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (108)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (126)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (169)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (192)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (217)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (219)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (221)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (235)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (342)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (345)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (346)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (360)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (374)  
<223> n equals a,t,g, or c

<400> 390  
tcaangcgca attaacccctc actaaaggga acaaaagctg ggaacgatct ggtntctctg 60  
cgcgctgcnc gcacactgag gccgcccggg acaaagcccg gnntcgngc gacctttggt 120  
cccggntca gtgagcgagc gagcgcgag agagggagt gccaactna tcactagggg 180  
ttccttgtag tnaatgatta acccgccatg ctacttngnc nacgtagcca tgggntacca 240  
agctcgagct ctctagactc gacgcgcgta atacgactca ctatagggcg aatttgagct 300  
ccaccgcggt tgcggccgct ctactagagt cgacctcatg gnttncccc gaaacccgcg 360  
aacaccgcgt gacncgcct ta 382

<210> 391  
<211> 375  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (6)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (7)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (48)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (70)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (104)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (117)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (138)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (146)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (159)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (208)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (223)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (261)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (269)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (275)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (279)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (299)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (351)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (366)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (370)

<223> n equals a,t,g, or c

<400> 391

```
tgcaannгаа tacacactaa ggacaagtgg actcacggtg cgccctcnga ctagtggtcc 60
cgggtgcagn tgccaggggtg gcctgagcga tctacggatg ggcngtatgg agtggangag 120
acgagatgcg ggtgttanag cagggnctga ccggagtgnс acacatgagt gtcaggtgca 180
ggtagtccga gtcggcgaca tgagcctnga gtagagtcат cantcgatga gatctggagg 240
caactggcga gcaagaccgt ntgggtgcant gtcantcang ctgttgсagg tgagagcant 300
gcactcgtcg agtggcgaga cagatcaatc tctgttagcg ggtggagggt ncactcgсgс 360
tgtgngggtн cactg 375
```

<210> 392

<211> 121

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (9)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (13)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (56)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (67)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (113)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (118)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (120)  
<223> n equals a,t,g, or c

<400> 392  
gantcatcng agngtgtgga ttgagccgc cgcatttttt aaccctaaat ctcganatgc 60  
atcgtgnttc ctgtccattg gactgtaagg ttatgtagg catcttgga acnatggan 120  
a 121

<210> 393  
<211> 83  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (65)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (66)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (70)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (73)  
<223> n equals a,t,g, or c

<400> 393  
ggcagagaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60  
aaaanncccn ggngggggcc ccc 83

<210> 394  
<211> 218  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (13)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (64)  
<223> n equals a,t,g, or c

<400> 394  
gtcggcgcag aangcgcccc gcacccccgc caggcgcatg tctgcacctc cgcttgccaa 60  
aggnctcgcg tcagcgactg gatgctcgcc atcaagggtcc agtgaagtt cttcaagagg 120  
aaaggcgccc ccgccccagg cttccgcgcc cagcgctcgc cacgctcagt gcccgtttta 180  
ccaataaact gagcgacccc aaaaaaaaaa aaaaaaag 218

<210> 395  
<211> 83  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (11)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (13)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (83)  
<223> n equals a,t,g, or c

<400> 395  
aattcggcac ngnaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60

aaaaaaaaaa aaaaaaaaaa aan

83

<210> 396

<211> 70

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (69)

<223> n equals a,t,g, or c

<400> 396

aattcggcac agaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60  
aaaaaaaaana 70

<210> 397

<211> 140

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (50)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (57)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (74)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (93)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (113)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (114)

<223> n equals a,t,g, or c



<220>  
<221> misc feature  
<222> (115)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (139)  
<223> n equals a,t,g, or c

<400> 397  
aatttgacca gagaacaaga ataaccggc ctcagcgccg ggttttcttn gcctcangat 60  
cgcccccaaa acanataacc aattgtattt atngaaaaat aaatagatac aannnactaa 120  
acatagcaat tcagatctnt 140

<210> 398  
<211> 157  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (10)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (65)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (121)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (122)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (123)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (126)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (134)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (150)  
<223> n equals a,t,g, or c

<400> 398  
aattcggcan agctcaagca gacggggctc aaggggggta catttaataa aaggatgaag 60  
atggnaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120  
nnnccngggg gggncceccc ccccccttn cccctt 157

<210> 399  
<211> 358  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (5)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (84)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (204)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (207)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (302)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (305)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (308)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (331)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (341)

<223> n equals a,t,g, or c

<400> 399

```
ggcanagcgg cagaggcggc tcccactctc ggaaccttgt cctgtttttc cccagctcg 60
gcaagcgcca tatgagcctg gcgncgcca tagcgaatcc tgttggtggc tttttggcct 120
attcccggcc ctgagtcctg ccgggatggc accgcccga taggacttcc agggttgggc 180
tgagtgggag ttcgactgct gggncctngta attctcgctt tgggggctgc tccttccagg 240
ctggggacac actggggccc gttgttcggt ctcccgctct ccgacatctt gtctggaact 300
tncgncctngc agtttccata ggagttggag nctgtgcggc ntaattttgg tggaaaaa 358
```

<210> 400

<211> 399

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (15)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (27)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (33)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (46)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (70)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (83)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (115)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (117)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (169)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (171)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (213)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (216)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (218)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (231)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (239)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (245)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (248)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (255)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (262)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (269)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (279)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (283)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (292)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (316)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (325)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (349)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (364)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (382)

<223> n equals a,t,g, or c

<400> 400

```
tttttttttt ttttnaaaag ggcacanata cantttttacc gtttanacca aaccagaatc 60
aaaacccaan tcagagtatc canaaatcca agccagggtca aaaccaaaac gaaantntca 120
agcaatccaa atcaagtcaa aaacaaaaac caaagtgccg gtacaggcnt nccgtgggtg 180
atcaggccac ccttccactc aaatggagtg ggnaantncc aaagactagt nttaccaant 240
ttcanatntc cggantccaa gngcctgtnc cttcccagng ttnagccgct gnattgatcc 300
tctgtggggg cctgcnaaac gccantctgg cgagggtgtc cactggggna attgcctacc 360
cggnagtgtc ctcaggttct gngtccctca agctggcca 399
```

<210> 401

<211> 189

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (11)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (162)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (165)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (166)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (187)

<223> n equals a,t,g, or c

<400> 401

```
naattcggca nagcaaacca caccttctct ttcttatgtc tttttactac aaactacaag 60
acaattgttg aaacctgcta tacatgttta ttttaataaa ttgatggcaa aaaaaaaaaa 120
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa anccnngggg ggggcccccc 180
ccccccntt                                     189
```

<210> 402

<211> 174

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (10)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (73)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (103)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (107)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (130)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (132)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (146)

<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (149)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (167)  
<223> n equals a,t,g, or c

<400> 402  
aattcggcan agctgaggca ggagaatcgc ttgaattcgg gaggcagagc tgagatcaca 60  
cctctgacac tcnagcctgg gtgacagagc gagactccgt cttaggnaag gaaaaaaaaa 120  
aaaaaaaaan cncggggggg gcccngtnc ccaattggcc ctatagnggg tcgt 174

<210> 403  
<211> 263  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (5)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (231)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (236)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (242)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (252)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (260)  
<223> n equals a,t,g, or c



<400> 403  
ggcanagcca acccagcagt ccttccctca gctgcctagg aggaagggac ccagctgggt 60  
ctgggaccac aaggaggag actgcacccc actgcctctg ggccctggct gtgggcagag 120  
gccaccgtgt gtgtcccgag taaccgtgcc gttgtcgtgt gatgccataa gcgtctgtgc 180  
gtggagtccc caatgaaacc tgtggctcctg cctgggcaaa aaaaaaaaaa naaaanaaaa 240  
anaaagaaaa anaanaaan aaa 263

<210> 404  
<211> 478  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (159)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (259)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (427)  
<223> n equals a,t,g, or c

<400> 404  
tcgaccacag cgtccggggg ctgcagcatg ttgctgagga gtgaggaata gttgagcccc 60  
aagtctgaa gaggcggggc agccaggctg acatctgtgt ttcaagtggg gctcgccatg 120  
ccgggggttc ataggtcact ggctctccaa gtgccagang tgggcagggt gtggcactga 180  
gcccccccaa cactgtgccc tgggtggagaa agcactgacc tgtcatgccc cctcaaacc 240  
tcctctcttg acgtgcctnt tgcacccctc ccattaggac aatcagtccc ctcccatctg 300  
ggagtcacct ttctttttct accctagcca ttcttggtac ccagccatct gcccaagggt 360  
gccccctect ctcccatccc cctgccctcg tgggcagccc ggctggtttt gtaaagtgtg 420  
gttgtgnaca gtgatttttt cttgtattta aaaaaggcca gcattgtggt tcattaaa 478

<210> 405  
<211> 223  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (147)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (158)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (172)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (217)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (223)  
<223> n equals a,t,g, or c

<400> 405  
agacagcagg acggtggcca tggaagtcgg aatccgctaa ggagtgtgta acaactcacc 60  
tgccgaatca actagccctg aaaatggatg gcgctggagc gtcggggcca tacccgctcg 120  
tcgccggcag tcgagagtgg acggggancgg cgggggcngc gcgcgcgcgc gncgtgatgg 180  
tgtgcgtcgg agggcggcgg cggcggcggg ggtgtgnggt ccn 223

<210> 406  
<211> 104  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (8)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (37)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (81)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (93)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (103)  
<223> n equals a,t,g, or c

357

<400> 406  
cccacgcntc cgccgacagc agcagcctca ccatgagtt gctgatggtc ctcagtctgg 60  
cggccctctc ccagcactgc nacgcaggct ctngctgccc ctna 104

<210> 407  
<211> 66  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (17)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (21)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (57)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (66)  
<223> n equals a,t,g, or c

<400> 407  
gccctatagt gagtctngta ncaattcact ggccgctcgtt ttacaacgtc gtgacgngga 60  
aaactn 66

<210> 408  
<211> 278  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (6)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (19)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature

<222> (252)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (275)

<223> n equals a,t,g, or c

<400> 408

```
gggcanagca agctcctgna cctcaagtga tccacatgcc ttggttgacc aaattgctgg 60
gattacaggc atgagccaat atgaccagct caaacatctt ctttttaa at gtcagaagca 120
tgtatagtga ttatttctta ttttttcccc ctgatccat ctcaccagat gtttggtgat 180
tttataagaa ttttcaaact accagcttct ggctttgttg aacttgggat ttctgtttca 240
ctaattttct tntcctgtgc ttgtacttac tttgntgg 278
```

<210> 409

<211> 168

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (16)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (38)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (127)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (140)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (143)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (145)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (167)

<223> n equals a,t,g, or c

<400> 409

```
aataaaactc taaaangatc actataaaaa aagcaggnac gcctgcaggt accggtccgg 60
aattccccggg tcgaccacg cgtccgacgg ctgcgagaag acgacagaag ggcacggctg 120
cgagaanacg acagaagggn gcnantgaaa gaaggcgga gaaaggnt 168
```

<210> 410

<211> 415

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (307)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (347)

<223> n equals a,t,g, or c

<400> 410

```
tgaataccta agatttctgt cttgggggtt ttggtgcatg cagttgatta cttcttattt 60
ttcttaccac ttgtgaatgt tgggtgtgaaa caattaatga agcttttgaa tcatccctat 120
tctgtgtttt atctagtcac ataaatggat taattactaa ttccagttga gaccttctaa 180
ttggttttta ctgaaacatt gaggggaacac aaatttatgg gcttcctgat gatgattctt 240
ctaggcatca tgtcctatag ttgtcatcc ctgatgaatg taaaattaca ctgttcacaa 300
aggtttngtc tcctttccac tgctattaat catggtcact ctcccnaaa tattatattt 360
tttctattaa aagaaaaaaaaa tggaaaaaaaaa ttacaaggca atggaaacta ttata 415
```

<210> 411

<211> 636

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (383)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (512)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (519)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (544)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (547)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (583)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (599)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (603)

<223> n equals a,t,g, or c

<400> 411

```
gcagatcaga cggtggcgacc cgctgaattt aagcatatta gtcagcggag gagaagaaac 60
taaccaggat tccctcagta acggcgagtg aacagggaag agcccagcgc cgaatccccg 120
cccccgggcg gggcgcgagg catgtggcgt acggaagacc cgctccccgg cgccgctcgt 180
ggggggccca agtccttctg atcgaggccc agcccgtgga cgggtgtgagg ccggtagcgg 240
ccccgggcgc gccgggcccg ggtcttcccg gagtcggggt gcttggggaat gcagcccaaa 300
gcgggtggta aactccatct aaggctaaat ccccttgtaa atttaactgt tagtccaaag 360
aggaacagct ctttgacac tangaaaaaa ctttgtagag agagtaaaaa atttaacacc 420
catagtaggc ctaaaagcag ccaccaatta agaaagcgtt caagctcaac acccactacc 480
taaaaaatcc caaacatata actgaactcc tnacaccna ttggaccaat ctatcaccc 540
atanaanaac taatggtagt ataagtaaca tgaaaacatt ctnccttcgca taagcctgng 600
tanattaataa cacttgaact gaccattaac aggcca 636
```

<210> 412

<211> 182

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (129)

<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (166)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (169)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (170)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (172)  
<223> n equals a,t,g, or c

<400> 412  
ccattgattt ttatcaatag tcgtattcat acggatagtc ctggtattgt tccatcacat 60  
tctgaggatg ctcttcgaac tcttcaaatt cttcttccat atatcacctt aaatagtgga 120  
ttgcggtant aaagattgtg cctgtctttt aaccacatca ggctcngann gntctcgtga 180  
ac 182

<210> 413  
<211> 387  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (157)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (253)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (317)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (323)  
<223> n equals a,t,g, or c

<220>

<221> misc feature  
<222> (349)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (351)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (364)  
<223> n equals a,t,g, or c

<400> 413  
tcgacccacg cgtccgccc cgcgtccgcc aagaccaccc tcctttcatt tgctagaagg 60  
actcactaga ctcaggaaag ctgttaggct cacagttaca gtttattaca gtaaaaggac 120  
agagattaag atcagcaaag ggaggagggtg cacagcnacg ttccacgaca gatgaggcga 180  
cgggttccat ctgccctctc ccagtggagc catataggca gcacctgatt ctcacagcaa 240  
catgtgacaa canccaagaa gtactgccaa tactgccaac cagagcagct tcaactcggag 300  
atctttgtgt tccaganttt ttngtttgtc ttggagacag ggtctgggnc ngtttgggca 360  
gacnaagagt acatggtgga gattcac 387

<210> 414  
<211> 276  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (60)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (186)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (195)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (237)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (260)



<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (266)

<223> n equals a,t,g, or c

<400> 414

```
gcaaaggtcc atactgggta cttgggtttca ttgccaccac ttagtggatg ttcagtttan 60
aaccattttg tctgctccct ctggaagcct tgcgcatagc ttactttgta attgttggag 120
aataactgct gaatttttag ctgttttgag ttgattcgca ccaactgcacc acaactcact 180
atgaanacta tttancttat ttattatctt gtgaaaagta taccatgaaa attttgntca 240
tactgtattt atcaagtatn attaanagca ctagat                                276
```

<210> 415

<211> 192

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (78)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (88)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (99)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (145)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (150)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (164)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (168)

<223> n equals a,t,g, or c

<400> 415

```
aaaagattgg actaagacac tggccatacc actggacagg gttatgttaa cacctgaaat 60
tgctgggtct tgagagancc caacgcantt ctgggagang gaccacattg gggggtaggt 120
ccacgggctt ggtgatagaa ttatntotcn atcgacttct tgantgcnat atgaactgta 180
acatttgctt ag 192
```

<210> 416

<211> 439

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (7)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (9)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (64)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (406)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (417)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (421)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (431)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (434)

<223> n equals a,t,g, or c

<400> 416

```
gcgagantnc gacagaaggg tacggctgcg agagacgaca gaaggggtacg gctgcgagaa 60
gacnacagaa ggggtacggct gcgagaagac gacagaaggg tacggctgcg agaagacgac 120
agaaggggtac ggctgcgaga agacgacaga aggtacggct gcgagaagac gacagaagga 180
tacggctgcg agaagacgac agaagggaga atcttagttc aactttaaat ttgcccacag 240
aaccctctaa atccccctgt aaatttaact gttagtccaa agaggaacag ctctttggac 300
actaggaaaa aaccttgtag agagagtaaa aaatttaaca cccatagtag gcctaaaagc 360
agccaccaat taagaaagcg ttcaaagctc aacaccact acccanaaaa taaaaanaaa 420
naaaaaccgc nggnccgct 439
```

<210> 417

<211> 155

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (9)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (84)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (122)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (123)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (143)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (153)

<223> n equals a,t,g, or c

<400> 417

```
gacatcttnt tggtttttat ttgaaacaa ttttaggct tgttccggg gtctctgtgc 60
tgctgtact gtattgacct gttntatagg tgccttttta taaaaagaa aattcaaaaa 120
```

annaaaaaaaa aaattaataa aaaaaaaaaa aanca

155

<210> 418

<211> 291

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (285)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (286)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (288)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (289)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (291)

<223> n equals a,t,g, or c

<400> 418

gaaaaaagaa atccatatct taaagaaaca gctttcaagt gcctttctgc agtttttcag 60  
gagcgcaaga tagatttgga ataggaataa gctctagttc ttaacaaccg acactcctac 120  
aagatttaga aaaaagttta caacataatc tagtttacag aaaaatcttg tgctagaata 180  
ctttttaaaa ggtattttga ataccattaa aactgctttt ttttttccag caagtatcca 240  
accaacttgg ttctgcttca ataaatcttt ggaaaaacta atttnnanna n 291

<210> 419

<211> 340

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (2)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

367

&lt;222&gt; (315)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 419

Val	Xaa	Asp	Trp	Phe	Leu	Trp	Tyr	Val	Lys	Lys	Cys	Gly	Gly	Thr	Thr
1				5					10					15	

Arg	Ile	Ile	Ser	Thr	Thr	Asn	Gly	Gly	Gln	Glu	Arg	Lys	Phe	Val	Gly
			20					25						30	

Gly	Ser	Gly	Gln	Val	Ser	Glu	Arg	Ile	Met	Asp	Leu	Leu	Gly	Asp	Arg
		35						40					45		

Val	Lys	Leu	Glu	Arg	Pro	Val	Ile	Tyr	Ile	Asp	Gln	Thr	Arg	Glu	Asn
	50						55				60				

Val	Leu	Val	Glu	Thr	Leu	Asn	His	Glu	Met	Tyr	Glu	Ala	Lys	Tyr	Val
65					70					75					80

Ile	Ser	Ala	Ile	Pro	Pro	Thr	Leu	Gly	Met	Lys	Ile	His	Phe	Asn	Pro
				85					90					95	

Pro	Leu	Pro	Met	Met	Arg	Asn	Gln	Met	Ile	Thr	Arg	Val	Pro	Leu	Gly
			100					105					110		

Ser	Val	Ile	Lys	Cys	Ile	Val	Tyr	Tyr	Lys	Glu	Pro	Phe	Trp	Arg	Lys
		115					120						125		

Lys	Asp	Tyr	Cys	Gly	Thr	Met	Ile	Ile	Asp	Gly	Glu	Glu	Ala	Pro	Val
	130					135					140				

Ala	Tyr	Thr	Leu	Asp	Asp	Thr	Lys	Pro	Glu	Gly	Asn	Tyr	Ala	Ala	Ile
145					150					155					160

Met	Gly	Phe	Ile	Leu	Ala	His	Lys	Ala	Arg	Lys	Leu	Ala	Arg	Leu	Thr
			165						170					175	

Lys	Glu	Glu	Arg	Leu	Lys	Lys	Leu	Cys	Glu	Leu	Tyr	Ala	Lys	Val	Leu
			180					185					190		

Gly	Ser	Leu	Glu	Ala	Leu	Glu	Pro	Val	His	Tyr	Glu	Glu	Lys	Asn	Trp
		195					200						205		

Cys	Glu	Glu	Gln	Tyr	Ser	Gly	Gly	Cys	Tyr	Thr	Thr	Tyr	Phe	Pro	Pro
	210					215					220				

Gly	Ile	Leu	Thr	Gln	Tyr	Gly	Arg	Val	Leu	Arg	Gln	Pro	Val	Asp	Arg
225				230						235					240

Ile	Tyr	Phe	Ala	Gly	Thr	Glu	Thr	Ala	Thr	His	Trp	Ser	Gly	Tyr	Met
			245						250					255	

368

Glu Gly Ala Val Glu Ala Gly Glu Arg Ala Ala Arg Glu Ile Leu His  
                   260                  265                  270

Ala Met Gly Lys Ile Pro Glu Asp Glu Ile Trp Gln Ser Glu Pro Glu  
                   275                  280                  285

Ser Val Asp Val Pro Ala Gln Pro Ile Thr Thr Thr Phe Leu Glu Arg  
                   290                  295                  300

His Leu Pro Ser Val Pro Gly Leu Leu Arg Xaa Ile Gly Leu Thr Thr  
                   305                  310                  315                  320

Ile Phe Ser Ala Thr Ala Leu Gly Phe Leu Ala His Lys Arg Gly Leu  
                   325                  330                  335

Leu Val Arg Val  
                   340

&lt;210&gt; 420

&lt;211&gt; 111

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (48)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 420

Thr Arg Asp Leu Val Ser Phe Ile Ser Gly Ile Arg Leu Tyr Asn Leu  
                   1                  5                  10                  15

Met Leu Ser Val Leu Arg His Lys Arg Gln Asn Val Ala Tyr Phe Arg  
                   20                  25                  30

Ile Cys Phe Phe Ile Glu Val Ser Gly Ile Leu Ser Lys Ile Val Xaa  
                   35                  40                  45

Ser Arg His Cys Ser Leu Cys Ser Ser Gly Thr Ser Cys Pro Leu Leu  
                   50                  55                  60

Ser Leu Gln Ala Thr Gly Asn Ala Ser Val Leu Val Ser Trp Arg Lys  
                   65                  70                  75                  80

Ile Thr Trp Gly Glu Gly Thr Ser Cys Gly Lys Ser Lys Cys Arg Tyr  
                   85                  90                  95

Glu Met Arg Arg Leu Pro Gln Leu Lys Val Asp Lys Ser Ala Leu

369

100

105

110

&lt;210&gt; 421

&lt;211&gt; 61

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (1)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 421

Xaa Ile Trp Cys Ile Ile Cys Lys Glu Ser Lys Met Met Ser Phe Pro  
1 5 10 15

Arg Gly Met Asn Leu Arg Asn Ala Phe Asp Gly Asp Val Ser Val Thr  
20 25 30

Leu Cys Tyr Ser Gly Ser Ser Asn Asn Ser Lys Ala Asn Tyr Ser Lys  
35 40 45

Cys Lys Ile Phe Leu Phe Pro Arg Phe Thr Phe Val Trp  
50 55 60

&lt;210&gt; 422

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 422

Thr His Ala Tyr Cys Ser Asn Leu Ser Phe Arg Leu Tyr Asp Gln Trp  
1 5 10 15

Arg Ala Trp Met Gln Lys Ser His Lys Thr Arg Asn Gln His Arg Thr  
20 25 30

Arg Gly Ser Cys Pro Arg Ala Asp Gly Ala Arg Arg Glu Val Leu Pro  
35 40 45

Asp Lys Leu  
50

&lt;210&gt; 423

&lt;211&gt; 246

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (71)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (101)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (117)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (147)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 423

Thr	Arg	Asn	Asp	Met	Lys	Ala	Asp	Cys	Ile	Leu	Tyr	Tyr	Gly	Phe	Gly
1				5					10					15	

Asp	Ile	Phe	Arg	Ile	Ser	Ser	Met	Val	Val	Met	Glu	Asn	Val	Gly	Gln
			20					25					30		

Gln	Lys	Leu	Tyr	Glu	Met	Val	Ser	Tyr	Cys	Gln	Asn	Ile	Ser	Lys	Cys
	35						40					45			

Arg	Arg	Val	Leu	Met	Ala	Gln	His	Phe	Asp	Glu	Val	Trp	Asn	Ser	Glu
	50					55					60				

Ala	Cys	Asn	Lys	Met	Cys	Xaa	Asn	Cys	Cys	Lys	Asp	Ser	Ala	Phe	Glu
65					70					75					80

Arg	Lys	Asn	Ile	Thr	Glu	Tyr	Cys	Arg	Asp	Leu	Ile	Lys	Ile	Leu	Lys
			85						90					95	

Gln	Ala	Glu	Gly	Xaa	Gly	Met	Glu	Lys	Leu	Thr	Pro	Ile	Gly	Asn	Trp
		100						105					110		

Ile	Asp	Ser	Trp	Xaa	Gly	Lys	Gly	Ala	Ala	Lys	Leu	Arg	Val	Ala	Gly
		115					120					125			

Val	Val	Ala	Pro	Thr	Leu	Pro	Arg	Glu	Asp	Leu	Glu	Lys	Ile	Ile	Ala
		130				135						140			



371

His Phe Xaa Ile Gln Gln Tyr Leu Lys Glu Asp Tyr Ser Phe Thr Ala  
 145 150 155 160  
 Tyr Ala Thr Ile Ser Tyr Leu Lys Ile Gly Pro Lys Ala Asn Leu Leu  
 165 170 175  
 Asn Asn Glu Ala His Ala Ile Thr Met Gln Val Thr Lys Ser Thr Gln  
 180 185 190  
 Asn Ser Phe Arg Ala Glu Ser Ser Gln Thr Cys His Ser Glu Gln Gly  
 195 200 205  
 Asp Lys Lys Met Glu Glu Lys Asn Ser Gly Asn Phe Gln Lys Lys Ala  
 210 215 220  
 Ala Asn Met Leu Gln Gln Ser Gly Ser Lys Asn Thr Gly Ala Lys Lys  
 225 230 235 240  
 Arg Lys Ile Asp Asp Ala  
 245

&lt;210&gt; 424

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (77)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 424

Asp His Trp Pro Arg Pro Glu Trp Leu Pro Cys Thr Ser Trp Arg Arg  
 1 5 10 15  
 Ala Ser Cys Leu Asn His Val Asn Cys His His Leu Ala Thr Pro Ala  
 20 25 30  
 Pro Ala Ser Ala Leu Pro Pro Phe Pro Pro Ser Trp Ser Gly Gly Tyr  
 35 40 45  
 Arg Ser Leu Gly Pro Thr Leu Ala Pro Leu Ser Pro Ala Ser Val Cys  
 50 55 60  
 Leu Thr Val Phe Pro Pro Leu Pro Gln Leu Arg Cys Xaa Pro Gln Ala  
 65 70 75 80  
 Trp Cys Cys Leu Gly Gly Leu Gly Glu Gly Val Cys Gly Gly Gly Arg  
 85 90 95

372

Arg Val Lys Thr Glu Ala Arg Cys Gln Asn Gly Leu Glu  
 100 105

&lt;210&gt; 425

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (5)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (49)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 425

Gly Ser Glu Thr Xaa Lys Tyr Leu Val Glu Asp Lys Arg Leu Gly Leu  
 1 5 10 15

Tyr Thr Trp Leu Cys Thr Asp Leu Leu Ser His Ile Gly Asn His His  
 20 25 30

Thr Leu Gln Gly Ile Ser Phe Ile Cys Lys Met Gln Arg Leu Val Leu  
 35 40 45

Xaa Asn His Thr Asn Phe Phe Val Leu  
 50 55

&lt;210&gt; 426

&lt;211&gt; 99

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (96)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 426

Phe Gly Thr Ser Gly Asp Gly Gly Gly Ser Lys Met Ala Gln Ala Ile  
 1 5 10 15

Phe Glu Ala Leu Glu Gly Met Asp Asn Gln Thr Val Leu Ala Val Gln

373

20                      25                      30  
 Ser Leu Leu Asp Gly Gln Gly Ala Val Pro Asp Pro Thr Gly Gln Ser  
                     35                      40                      45  
 Val Asn Ala Pro Pro Ala Ile Gln Pro Leu Asp Asp Glu Asp Val Phe  
                     50                      55                      60  
 Leu Cys Gly Lys Cys Lys Lys Gln Phe Asn Ser Leu Pro Ala Phe Met  
                     65                      70                      75                      80  
 Thr His Lys Arg Glu Gln Cys Gln Gly Asn Ala Pro Ala Leu Ala Xaa  
                     85                      90                      95  
 Val Ser Leu

<210> 427  
 <211> 55  
 <212> PRT  
 <213> Homo sapiens

<400> 427  
 Asn Ser Asn Ser Ser Ile Phe Ser Leu Val Ser Val Lys Cys Asp Lys  
                     1                      5                      10                      15  
 Ser Thr Tyr Phe Lys Leu Phe Ser Ala Leu Gly Tyr Ser Ser Asn Lys  
                     20                      25                      30  
 Asn Thr Asn Leu Trp Val Phe Lys Lys Thr Trp Arg Ile Asn Ser Tyr  
                     35                      40                      45  
 Phe Lys Arg Ser Lys Lys Lys  
                     50                      55

<210> 428  
 <211> 54  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (41)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 428  
 His Thr Leu Ser Asn Leu Glu Phe Ala Gln Lys Val Glu Pro Cys Asn

374

1                    5                    10                    15  
 Asp His Val Arg Ala Lys Leu Ser Trp Ala Lys Lys Arg Asp Glu Asp  
                   20                    25                    30  
 Asp Val Pro Thr Val Pro Ser Thr Xaa Gly Glu Glu Arg Leu Tyr Asn  
                   35                    40                    45  
 Pro Phe Leu Arg Val Ala  
                   50

<210> 429  
 <211> 39  
 <212> PRT  
 <213> Homo sapiens

<400> 429  
 Arg Gln Thr Lys Val Asn Leu Lys Glu Thr Arg Ser Phe Glu Ile Ile  
   1                    5                    10                    15  
 Val Trp Gly Phe Tyr Lys Ser Asn Tyr Cys His Leu His Pro Asp Ser  
                   20                    25                    30  
 Phe Lys Leu Leu Ile His Pro  
                   35

<210> 430  
 <211> 133  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (81)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (85)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 430  
 Ala Arg Ala Pro Arg Val Pro Pro Ala Pro His Thr Pro Ser Lys Met  
   1                    5                    10                    15  
 Gly Lys Glu Lys Thr His Ile Asn Ile Val Val Ile Gly His Val Asp  
                   20                    25                    30

375

Ser Gly Lys Ser Thr Thr Thr Gly His Leu Ile Tyr Lys Cys Gly Gly  
           35                    40                    45  
 Ile Asp Lys Arg Thr Ile Glu Lys Phe Glu Lys Glu Ala Ala Glu Met  
           50                    55                    60  
 Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys Ala  
           65                    70                    75                    80  
 Xaa Val Ser Ala Xaa Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe Glu  
                     85                    90                    95  
 Thr Thr Lys Tyr Tyr Ile Thr Ile Ile Asp Ala Pro Gly His Arg Asp  
                     100                    105                    110  
 Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala Val  
           115                    120                    125  
 Leu Ile Val Ala Ala  
           130

<210> 431  
 <211> 190  
 <212> PRT  
 <213> Homo sapiens

<400> 431  
 Leu Cys Trp Ala Arg Pro Leu Pro Ser Gly Pro Val Leu Leu Ala Ala  
   1                    5                    10                    15  
 Asn Lys Asp Ser Ser Trp Cys Pro Thr Cys Leu Val His Cys Cys Val  
           20                    25                    30  
 Asn Pro Gly Gly Ser Gly His Arg Arg Gln Pro Arg Pro Arg Val Gln  
           35                    40                    45  
 Glu Lys Cys Ser Leu Glu Ala Arg Thr Thr Ala Ser His Trp Gly Arg  
           50                    55                    60  
 Arg Gly Pro Arg Thr Thr Ser Ala Ser Tyr Leu Pro Ala Ser Ala Arg  
           65                    70                    75                    80  
 Gly Pro Arg Asp Ala Val Leu Phe Gln Pro Pro Ala Leu Gly Arg Gly  
                     85                    90                    95  
 His Ala Ser Arg Ile Gln Gly Ala Gly Gly Leu Ser Thr Ala Arg Thr  
           100                    105                    110

376

Cys Leu Leu Ala Ala Ala Val Gly Glu His Gly Gly Cys Gln Arg  
 115 120 125

Leu Leu Trp Lys Val Ala Ala Ser Glu Met Ala Gly Ala Ala Gly Val  
 130 135 140

Arg Leu His Thr Ala Gln Val Ser Ser Gly Arg Leu Ser Trp Gly Gly  
 145 150 155 160

Ser Ser Ser Ala Glu Gly Trp Trp Gly Val Gln Ser Val Ile Leu Gly  
 165 170 175

Ala Val Cys Pro Thr Pro Ala Trp Gly Pro His Phe Arg Arg  
 180 185 190

&lt;210&gt; 432

&lt;211&gt; 310

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 432

Gly Pro His Gly Asn Gly Glu Val Arg Trp Pro Leu Pro Pro Pro Pro  
 1 5 10 15

Pro Arg Phe Val Ala Arg Arg Lys Met Ala Asp Leu Glu Glu Gln Leu  
 20 25 30

Ser Asp Glu Glu Lys Val Arg Ile Ala Ala Lys Phe Ile Ile His Ala  
 35 40 45

Pro Pro Gly Glu Phe Asn Glu Val Phe Asn Asp Val Arg Leu Leu Leu  
 50 55 60

Asn Asn Asp Asn Leu Leu Arg Glu Gly Ala Ala His Ala Phe Ala Gln  
 65 70 75 80

Tyr Asn Leu Asp Gln Phe Thr Pro Val Lys Ile Glu Gly Tyr Glu Asp  
 85 90 95

Gln Val Leu Ile Thr Glu His Gly Asp Leu Gly Asn Gly Lys Phe Leu  
 100 105 110

Asp Pro Lys Asn Arg Ile Cys Phe Lys Phe Asp His Leu Arg Lys Glu  
 115 120 125

Ala Thr Asp Pro Arg Pro Cys Glu Val Glu Asn Ala Val Glu Ser Trp  
 130 135 140

Arg Thr Ser Val Glu Thr Ala Leu Arg Ala Tyr Val Lys Glu His Tyr

377

145	150	155	160
Pro Asn Gly Val Cys Thr Val Tyr Gly Lys Lys Ile Asp Gly Gln Gln			
	165	170	175
Thr Ile Ile Ala Cys Ile Glu Ser His Gln Phe Gln Ala Lys Asn Phe			
	180	185	190
Trp Asn Gly Arg Trp Arg Ser Glu Trp Lys Phe Thr Ile Thr Pro Ser			
	195	200	205
Thr Thr Gln Val Val Gly Ile Leu Lys Ile Gln Val His Tyr Tyr Glu			
	210	215	220
Asp Gly Asn Val Gln Leu Val Ser His Lys Asp Ile Gln Asp Ser Leu			
	225	230	235
Thr Val Ser Asn Glu Val Gln Thr Ala Lys Glu Phe Ile Lys Ile Val			
	245	250	255
Glu Ala Ala Glu Asn Glu Tyr Gln Thr Ala Ile Ser Glu Asn Tyr Gln			
	260	265	270
Thr Met Ser Asp Thr Thr Phe Lys Ala Leu Arg Arg Gln Leu Pro Val			
	275	280	285
Thr Arg Thr Lys Ile Asp Trp Asn Lys Ile Leu Ser Tyr Lys Ile Gly			
	290	295	300
Lys Glu Met Gln Asn Ala			
	305	310	

&lt;210&gt; 433

&lt;211&gt; 289

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (287)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (288)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 433

Gln Ser Cys Thr Ser Gly Ser Ser Lys Pro Asn Ser Pro Ser Ile Ser

378

1	5	10	15
Pro Ser Ile Leu Ser Asn Thr Glu His Lys Arg Gly Pro Glu Val Thr	20	25	30
Ser Gln Gly Val Gln Thr Ser Ser Pro Ala Cys Lys Gln Glu Lys Asp	35	40	45
Asp Lys Glu Glu Lys Lys Asp Ala Ala Glu Gln Val Arg Lys Ser Thr	50	55	60
Leu Asn Pro Asn Ala Lys Glu Phe Asn Pro Arg Ser Phe Ser Gln Pro	65	70	75
Lys Pro Ser Thr Thr Pro Thr Ser Pro Arg Pro Gln Ala Gln Pro Ser	85	90	95
Pro Ser Met Val Gly His Gln Gln Pro Thr Pro Val Tyr Thr Gln Pro	100	105	110
Val Cys Phe Ala Pro Asn Met Met Tyr Pro Val Pro Val Ser Pro Gly	115	120	125
Val Gln Pro Leu Tyr Pro Ile Pro Met Thr Pro Met Pro Val Asn Gln	130	135	140
Ala Lys Thr Tyr Arg Ala Gly Lys Val Pro Asn Met Pro Gln Gln Arg	145	150	155
Gln Asp Gln His His Gln Ser Ala Met Met His Pro Ala Ser Ala Ala	165	170	175
Gly Pro Pro Ile Ala Ala Thr Pro Pro Ala Tyr Ser Thr Gln Tyr Val	180	185	190
Ala Tyr Ser Pro Gln Gln Phe Pro Asn Gln Pro Leu Val Gln His Val	195	200	205
Pro His Tyr Gln Ser Gln His Pro His Val Tyr Ser Pro Val Ile Gln	210	215	220
Gly Asn Ala Arg Met Met Ala Pro Pro Thr His Ala Gln Pro Gly Leu	225	230	235
Val Ser Ser Ser Ala Thr Gln Tyr Gly Ala His Glu Gln Thr His Ala	245	250	255
Met Tyr Ala Cys Pro Lys Leu Pro Tyr Asn Lys Glu Thr Ser Pro Ser	260	265	270
Phe Tyr Phe Ala Ile Ser Thr Gly Ser Leu Ala Gln Gln Tyr Xaa Xaa			



379

275

280

285

Pro

&lt;210&gt; 434

&lt;211&gt; 147

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 434

Lys Val Thr Pro Asp Leu Lys Pro Thr Glu Ala Ser Ser Ser Ala Phe  
 1 5 10 15

Arg Leu Met Pro Ala Leu Gly Val Ser Val Ala Asp Gln Lys Gly Lys  
 20 25 30

Ser Thr Val Ala Ser Ser Glu Ala Lys Pro Ala Ala Thr Ile Arg Ile  
 35 40 45

Val Gln Gly Leu Gly Val Met Pro Pro Lys Ala Gly Gln Thr Ile Thr  
 50 55 60

Val Ala Thr His Ala Lys Gln Gly Ala Ser Val Ala Ser Gly Ser Gly  
 65 70 75 80

Thr Val His Thr Ser Ala Val Ser Leu Pro Ser Met Asn Ala Ala Val  
 85 90 95

Ser Lys Thr Val Ala Val Ala Ser Gly Ala Ala Arg Pro Pro Ser Ala  
 100 105 110

Ser Ala Gln Glu Pro Pro Pro Cys Gly Arg Ser Leu Ser Ala Pro Arg  
 115 120 125

Leu Cys Pro Arg Pro Arg Leu Gly Ser Cys Leu His Gly Ser Gln Phe  
 130 135 140

Pro Ser Leu  
 145

&lt;210&gt; 435

&lt;211&gt; 151

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

380

&lt;221&gt; SITE

&lt;222&gt; (9)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (15)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (79)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 435

Gly	Ser	Gly	Thr	Lys	Asp	Pro	Ser	Xaa	Cys	Asn	Thr	Gln	Thr	Xaa	Ala
1				5				10						15	

His	Thr	His	Thr	Gly	Gly	Glu	Ile	Ser	Leu	Phe	Ser	Met	Ser	Phe	Phe
			20					25					30		

Ser	Trp	Ala	Glu	Thr	Gly	Tyr	Cys	Pro	Gly	Gln	Leu	Pro	Glu	Lys	His
		35					40					45			

Arg	Arg	Glu	Leu	Arg	Ser	Ala	Arg	Pro	Ser	Ser	Leu	Ala	Pro	Gly	Phe
		50				55					60				

Gly	Gly	Pro	Arg	Thr	Ala	Asp	Arg	Gly	Trp	Ser	Trp	Arg	Leu	Xaa	Ser
	65				70					75					80

Arg	Ala	Tyr	Thr	Trp	Arg	Asn	Ala	Pro	Pro	Ser	Ser	Pro	Ser	Leu	Gln
				85					90					95	

Thr	Trp	Gly	Trp	Leu	Gly	Pro	Glu	Gly	Cys	Asp	Glu	Glu	Lys	Arg	Ala
		100					105						110		

Ser	Val	Gly	Met	Arg	Gln	Glu	Gly	Ile	Asp	Phe	Asp	Cys	Asp	Leu	Trp
		115				120					125				

Gly	Phe	Leu	Pro	Ala	Leu	Asp	Asn	Pro	Ala	Lys	Asp	Cys	Phe	Phe	Leu
	130					135					140				

Ser	Leu	Ala	Arg	Arg	Gly	Pro
145					150	

&lt;210&gt; 436

&lt;211&gt; 180

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

381

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (42)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (123)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 436

Ala Pro Ala Ser Pro Val Met Pro Pro Gln Thr Gln Ser Pro Gly Gln  
 1 5 10 15

Pro Ala Gln Pro Ala Pro Met Val Pro Leu His Gln Lys Gln Ser Arg  
 20 25 30

Ile Thr Pro Ile Gln Lys Pro Arg Gly Xaa Asp Pro Val Glu Ile Leu  
 35 40 45

Gln Glu Arg Glu Tyr Arg Leu Gln Ala Arg Ile Ala His Arg Ile Gln  
 50 55 60

Glu Leu Glu Asn Leu Pro Gly Ser Leu Ala Gly Asp Leu Arg Thr Lys  
 65 70 75 80

Ala Thr Ile Glu Leu Lys Ala Leu Arg Leu Leu Asn Phe Gln Arg Gln  
 85 90 95

Leu Arg Gln Glu Val Val Val Cys Met Arg Arg Asp Thr Ala Leu Glu  
 100 105 110

Thr Ala Leu Asn Ala Lys Ala Tyr Lys Arg Xaa Ser Ala Ser Pro Cys  
 115 120 125

Ala Arg Pro Ala Ser Leu Arg Ser Trp Arg Ser Ser Arg Arg Ser Ser  
 130 135 140

Arg Ser Ala Ser Ala Gly Arg Ser Thr Arg Asn Thr Ser Ile Ala Phe  
 145 150 155 160

Ser Ser Met Pro Arg Ile Ser Arg Asn Ile Thr Asp Pro Ser Gln Ala  
 165 170 175

Lys Ser Arg Ser  
 180

&lt;210&gt; 437

382

<211> 415  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (8)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (94)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (96)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (170)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 437  
 Arg Lys Tyr Leu Val Pro Leu Xaa Lys Lys Leu Tyr Leu Lys Trp Ala  
           1                  5                  10                  15  
 Leu Glu Glu Tyr Leu Asp Glu Phe Asp Pro Cys His Cys Arg Pro Cys  
                   20                  25                  30  
 Gln Asn Gly Gly Leu Ala Thr Val Glu Gly Thr His Cys Leu Cys His  
                   35                  40                  45  
 Cys Lys Pro Tyr Thr Phe Gly Ala Ala Cys Glu Gln Gly Val Leu Val  
           50                  55                  60  
 Gly Asn Gln Ala Gly Gly Val Asp Gly Gly Trp Ser Cys Trp Ser Ser  
           65                  70                  75                  80  
 Trp Ser Pro Cys Val Gln Gly Lys Lys Thr Arg Ser Arg Xaa Cys Xaa  
                   85                  90                  95  
 Asn Pro Pro Pro Ser Gly Gly Gly Arg Ser Cys Val Gly Glu Thr Thr  
                   100                  105                  110  
 Glu Ser Thr Gln Cys Glu Asp Glu Glu Leu Glu His Leu Arg Leu Leu  
           115                  120                  125  
 Glu Pro His Cys Phe Pro Leu Ser Leu Val Pro Thr Glu Phe Cys Pro  
           130                  135                  140

383

Ser Pro Pro Ala Leu Lys Asp Gly Phe Val Gln Asp Glu Gly Thr Met  
 145 150 155 160

Phe Pro Val Gly Lys Asn Val Val Tyr Xaa Cys Asn Glu Gly Tyr Ser  
 165 170 175

Leu Ile Gly Asn Pro Val Ala Arg Cys Gly Glu Asp Leu Arg Trp Leu  
 180 185 190

Val Gly Glu Met His Cys Gln Lys Ile Ala Cys Val Leu Pro Val Leu  
 195 200 205

Met Asp Gly Ile Gln Ser His Pro Gln Lys Pro Phe Tyr Thr Val Gly  
 210 215 220

Glu Lys Val Thr Val Ser Cys Ser Gly Gly Met Ser Leu Glu Gly Pro  
 225 230 235 240

Ser Ala Phe Leu Cys Gly Ser Ser Leu Lys Trp Ser Pro Glu Met Lys  
 245 250 255

Asn Ala Arg Cys Val Gln Lys Glu Asn Pro Leu Thr Gln Ala Val Pro  
 260 265 270

Lys Cys Gln Arg Trp Glu Lys Leu Gln Asn Ser Arg Cys Val Cys Lys  
 275 280 285

Met Pro Tyr Glu Cys Gly Pro Ser Leu Asp Val Cys Ala Gln Asp Glu  
 290 295 300

Arg Ser Lys Arg Ile Leu Pro Leu Thr Val Cys Lys Met His Val Leu  
 305 310 315 320

His Cys Gln Gly Arg Asn Tyr Thr Leu Thr Gly Arg Asp Ser Cys Thr  
 325 330 335

Leu Pro Ala Ser Ala Glu Lys Ala Cys Gly Ala Cys Pro Leu Trp Gly  
 340 345 350

Lys Cys Asp Ala Glu Ser Ser Lys Cys Val Cys Arg Glu Ala Ser Glu  
 355 360 365

Cys Glu Glu Glu Gly Phe Ser Ile Cys Val Glu Val Asn Gly Lys Glu  
 370 375 380

Gln Thr Met Ser Glu Cys Glu Ala Gly Ala Leu Arg Cys Arg Gly Gln  
 385 390 395 400

Ser Ile Ser Val Thr Ser Ile Arg Pro Cys Ala Ala Glu Thr Gln  
 405 410 415

384

<210> 438  
 <211> 285  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (16)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (17)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (18)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 438  
 Leu Ile Arg Leu Thr Ile Gly Lys Ala Gly Ser Leu Gln Tyr Arg Xaa  
     1                    5                    10                    15  
  
 Xaa Xaa Phe Pro Gly Met Glu Ala Phe Leu Gly Ser Arg Ser Gly Leu  
                     20                    25                    30  
  
 Trp Ala Gly Gly Pro Ala Pro Gly Gln Phe Tyr Arg Ile Pro Ser Thr  
                     35                    40                    45  
  
 Pro Asp Ser Phe Met Asp Pro Ala Ser Ala Leu Tyr Arg Gly Pro Ile  
                     50                    55                    60  
  
 Thr Arg Thr Gln Asn Pro Met Val Thr Gly Thr Ser Val Leu Gly Val  
                     65                    70                    75                    80  
  
 Lys Phe Glu Gly Gly Val Val Ile Ala Ala Asp Met Leu Gly Ser Tyr  
                     85                    90                    95  
  
 Gly Ser Leu Ala Arg Phe Arg Asn Ile Ser Arg Ile Met Arg Val Asn  
                     100                    105                    110  
  
 Asn Ser Thr Met Leu Gly Ala Ser Gly Asp Tyr Ala Asp Phe Gln Tyr  
                     115                    120                    125  
  
 Leu Lys Gln Val Leu Gly Gln Met Val Ile Asp Glu Glu Leu Leu Gly  
                     130                    135                    140

385

Asp Gly His Ser Tyr Ser Pro Arg Ala Ile His Ser Trp Leu Thr Arg  
 145 150 155 160

Ala Met Tyr Ser Arg Arg Ser Lys Met Asn Pro Leu Trp Asn Thr Met  
 165 170 175

Val Ile Gly Gly Tyr Ala Asp Gly Glu Ser Phe Leu Gly Tyr Val Asp  
 180 185 190

Met Leu Gly Val Ala Tyr Glu Ala Pro Ser Leu Ala Thr Gly Tyr Gly  
 195 200 205

Ala Tyr Leu Ala Gln Pro Leu Leu Arg Glu Val Leu Glu Lys Gln Pro  
 210 215 220

Val Leu Ser Gln Thr Glu Ala Arg Asp Leu Val Glu Arg Cys Met Arg  
 225 230 235 240

Val Leu Tyr Tyr Arg Asp Ala Arg Ser Tyr Asn Arg Phe Gln Ile Ala  
 245 250 255

Thr Val Thr Glu Lys Gly Val Glu Ile Glu Gly Pro Leu Ser Thr Glu  
 260 265 270

Thr Asn Trp Asp Ile Ala His Met Ile Ser Gly Phe Glu  
 275 280 285

&lt;210&gt; 439

&lt;211&gt; 185

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 439

Asn Ser Ala Ala His Lys Lys Gly Lys Leu Pro Ile Val Asn Glu Asp  
 1 5 10 15

Asp Glu Leu Val Ala Ile Ile Ala Arg Thr Asp Leu Lys Lys Asn Arg  
 20 25 30

Asp Tyr Pro Leu Ala Ser Lys Asp Ala Lys Lys Gln Leu Leu Cys Gly  
 35 40 45

Ala Ala Ile Gly Thr His Glu Asp Asp Lys Tyr Arg Leu Asp Leu Leu  
 50 55 60

Ala Gln Ala Gly Val Asp Val Val Val Leu Asp Ser Ser Gln Gly Asn  
 65 70 75 80

Ser Ile Phe Gln Ile Asn Met Ile Lys Tyr Ile Lys Asp Lys Tyr Pro

386

	85		90		95
Asn Leu Gln Val Ile Gly Gly Asn Val Val Thr Ala Ala Gln Ala Lys					
	100		105		110
Asn Leu Ile Asp Ala Gly Val Asp Ala Leu Arg Val Gly Met Gly Ser					
	115		120		125
Gly Ser Ile Cys Ile Thr Gln Glu Val Leu Ala Cys Gly Arg Pro Gln					
	130		135		140
Ala Thr Ala Val Tyr Lys Val Ser Glu Tyr Ala Arg Arg Phe Gly Val					
	145		150		155
Pro Val Ile Ala Asp Gly Gly Ile Gln Asn Val Gly His Ile Ala Lys					
	165		170		175
Ala Leu Ala Leu Gly Ala Pro Gln Ser					
	180		185		

&lt;210&gt; 440

&lt;211&gt; 211

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 440

Leu Gln Gly Arg Ser Thr Pro Ile Trp Pro Ala Leu Ala Thr Val Thr					
1		5		10	15
Ser Arg Thr Pro Ala Leu Gly Pro Gln Ala Gly Ile Asp Thr Asn Glu					
	20		25		30
Ile Ala Pro Leu Glu Pro Asp Ala Pro Pro Asp Ala Cys Glu Ala Ser					
	35		40		45
Phe Asp Ala Val Ser Thr Ile Arg Gly Glu Leu Phe Phe Phe Lys Ala					
	50		55		60
Gly Phe Val Trp Arg Leu Arg Gly Gly Gln Leu Gln Pro Gly Tyr Pro					
	65		70		75
Ala Leu Ala Ser Arg His Trp Gln Gly Leu Pro Ser Pro Val Asp Ala					
	85		90		95
Ala Phe Glu Asp Ala Gln Gly His Ile Trp Phe Phe Gln Gly Ala Gln					
	100		105		110
Tyr Trp Val Tyr Asp Gly Glu Lys Pro Val Leu Gly Pro Ala Pro Leu					
	115		120		125



387

Thr Glu Leu Gly Leu Val Arg Phe Pro Val His Ala Ala Leu Val Trp  
 130 135 140

Gly Pro Glu Lys Asn Lys Ile Tyr Phe Phe Arg Gly Arg Asp Tyr Trp  
 145 150 155 160

Arg Phe His Pro Ser Thr Arg Arg Val Asp Ser Pro Val Pro Arg Arg  
 165 170 175

Pro Leu Thr Gly Glu Gly Cys Pro Leu Arg Ser Thr Leu Pro Ser Arg  
 180 185 190

Met Leu Met Ala Met Pro Thr Ser Cys Ala Ala Ala Ser Thr Gly Ser  
 195 200 205

Leu Thr Leu  
 210

<210> 441

<211> 80

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (40)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 441

Gly Gly Ala Gly Lys Leu Leu Ser Phe Thr His Ser Ala Pro Trp Ser  
 1 5 10 15

Arg Leu Trp Ser Ser Leu Gly Lys Arg Val Thr Gly Glu Ser Gln Gly  
 20 25 30

Leu Glu Lys Leu Pro Gly Thr Xaa Asp Gly Leu Ala Ala Leu Thr Gln  
 35 40 45

Asp Pro Leu Pro Leu Pro Pro Pro Leu Cys Arg Asn Thr Gly Thr Pro  
 50 55 60

Arg Gly Lys Met Ser Phe Ser Arg Leu Gln Phe Ser Pro Arg Lys Leu  
 65 70 75 80

388

<210> 442  
<211> 567  
<212> PRT  
<213> Homo sapiens

<220>  
<221> SITE  
<222> (205)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (212)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (469)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (503)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (505)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (517)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (535)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (546)  
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 442  
Asn Val His Leu Tyr Ile Met Tyr Tyr Met Glu Ala Lys His Ala Val  
1 5 10 15

Ser Phe Met Thr Cys Thr Gln Asn Val Ala Pro Asp Met Phe Arg Thr

389

20	25	30
Ile Pro Pro Glu Ala Asn Ile Pro Ile Pro Val Lys Ser Asp Met Val		
35	40	45
Met Met His Glu His His Lys Glu Thr Glu Tyr Lys Asp Lys Ile Pro		
50	55	60
Leu Leu Gln Gln Pro Lys Arg Glu Glu Glu Glu Val Leu Asp Gln Gly		
65	70	75
Asp Phe Tyr Ser Leu Leu Ser Lys Leu Leu Gly Glu Arg Glu Asp Val		
85	90	95
Val His Val His Lys Tyr Asn Pro Thr Glu Lys Ala Glu Ser Glu Ser		
100	105	110
Asp Leu Val Ala Glu Ile Ala Asn Val Val Gln Lys Lys Asp Leu Gly		
115	120	125
Arg Ser Asp Ala Arg Glu Gly Ala Glu His Glu Arg Gly Asn Ala Ile		
130	135	140
Leu Val Arg Asp Arg Ile His Lys Phe His Arg Leu Val Ser Thr Leu		
145	150	155
Arg Pro Pro Glu Ser Arg Val Phe Ser Leu Gln Gln Pro Pro Pro Gly		
165	170	175
Glu Gly Thr Trp Glu Pro Glu His Thr Gly Asp Phe His Met Glu Glu		
180	185	190
Ala Leu Asp Trp Pro Gly Val Tyr Leu Leu Pro Gly Xaa Val Ser Gly		
195	200	205
Val Ala Leu Xaa Pro Lys Asn Asn Leu Val Ile Phe His Arg Gly Asp		
210	215	220
His Val Trp Asp Gly Asn Ser Phe Asp Ser Lys Phe Val Tyr Gln Gln		
225	230	235
Ile Gly Leu Gly Pro Ile Glu Glu Asp Thr Ile Leu Val Ile Asp Pro		
245	250	255
Asn Asn Ala Ala Val Leu Gln Ser Ser Gly Lys Asn Leu Phe Tyr Leu		
260	265	270
Pro His Gly Leu Ser Ile Asp Lys Asp Gly Asn Tyr Trp Val Thr Asp		
275	280	285
Val Ala Leu His Gln Val Phe Lys Leu Asp Pro Asn Asn Lys Glu Gly		

390

290	295	300
Pro Val Leu Ile Leu Gly Arg Ser Met Gln Pro Gly Ser Asp Gln Asn		
305	310	315 320
His Phe Cys Gln Pro Thr Asp Val Ala Val Asp Pro Gly Thr Gly Ala		
	325	330 335
Ile Tyr Val Ser Asp Gly Tyr Cys Asn Ser Arg Ile Val Gln Phe Ser		
	340	345 350
Pro Ser Gly Lys Phe Ile Thr Gln Trp Gly Glu Glu Ser Ser Gly Ser		
	355	360 365
Ser Pro Leu Pro Gly Gln Phe Thr Val Pro His Ser Leu Ala Leu Val		
	370	375 380
Pro Leu Leu Gly Gln Leu Cys Val Ala Asp Arg Glu Asn Gly Arg Ile		
385	390	395 400
Gln Cys Phe Lys Thr Asp Thr Lys Glu Phe Val Arg Glu Ile Lys His		
	405	410 415
Ser Ser Phe Gly Arg Asn Val Phe Ala Ile Ser Tyr Ile Pro Gly Leu		
	420	425 430
Leu Phe Ala Val Asn Gly Lys Pro His Phe Gly Asp Gln Glu Pro Val		
	435	440 445
Gln Gly Phe Val Met Asn Phe Ser Asn Gly Glu Ile Ile Asp Ile Phe		
	450	455 460
Lys Pro Val Arg Xaa Leu Leu Asp Met Pro His Asp Ile Val Ala Ser		
465	470	475 480
Glu Asp Gly Thr Val Tyr Ile Gly Arg Cys Ser Tyr Gln His Arg Val		
	485	490 495
Gly Ser Ser Thr Leu Asp Xaa Arg Xaa Leu Gly Thr Ser Val Gln Phe		
	500	505 510
Lys Lys Gly Leu Xaa Ile Glu Val Gln Gly Asn Pro Lys Lys Pro Glu		
	515	520 525
Gly Ile Cys Cys Phe Pro Xaa Thr Thr Leu Arg Val Ile Pro Val Val		
	530	535 540
Gly Xaa Trp Arg Gly His Gly Pro Asn Leu Ile Pro Val Gly Lys Asn		
545	550	555 560
Pro Arg Gly Pro Leu Gly Arg		

391

565

<210> 443  
 <211> 129  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (123)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (127)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (129)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 443  
 Arg Pro Ser Cys Ser Pro Gly Ser Val Ser Ala Ala Ala Val Asn Met  
           1                  5                  10                  15

Glu Pro Pro Asp Ala Pro Ala Gln Ala Arg Gly Ala Pro Arg Leu Leu  
                   20                  25                  30

Leu Leu Ala Val Leu Leu Ala Ala His Pro Asp Ala Gln Ala Glu Val  
           35                  40                  45

Arg Leu Ser Val Pro Pro Leu Val Glu Val Met Arg Gly Lys Ser Val  
           50                  55                  60

Ile Leu Asp Cys Thr Pro Thr Gly Thr His Asp His Tyr Met Leu Glu  
       65                  70                  75                  80

Trp Phe Leu Thr Asp Arg Ser Gly Ala Arg Pro Arg Leu Ala Ser Ala  
                   85                  90                  95

Glu Met Gln Gly Ser Glu Leu Gln Val Thr Met His Asp Thr Arg Gly  
           100                  105                  110

Arg Ser Pro Pro Tyr Gln Leu Gly Leu Pro Xaa Gly Ala Trp Xaa Leu  
           115                  120                  125

Xaa

392

&lt;210&gt; 444

&lt;211&gt; 131

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 444

Glu Pro Arg Val Glu Arg Glu Thr Pro Gly Gln Pro Phe Ser Ser Ser  
 1 5 10 15

Phe Pro Ser Pro Ser Pro Phe Pro Asn Val Ala Ser Met Trp Val Leu  
 20 25 30

Gly Thr Trp Glu Lys Pro Leu Leu Cys His Phe Phe Ser Leu Phe Pro  
 35 40 45

Ser Ser Pro Pro Thr Val Trp Leu Met Met Ser Ser Gly Val Met Val  
 50 55 60

Thr Thr Pro Cys Ser Leu Phe Trp Tyr Phe Pro Cys Gln Phe Pro Leu  
 65 70 75 80

Ser Ala Arg Leu Cys Pro Lys Ile Pro Ser Ala Ser Ser Leu His Val  
 85 90 95

Ala Glu Gly Pro Gly Leu Pro Gln Val Pro Cys Leu Ser Asn Lys Val  
 100 105 110

Glu Thr Ile Lys Pro Gly Lys Lys Lys Gly Gly Arg Ser Lys Gly  
 115 120 125

Ser Pro Arg  
 130

&lt;210&gt; 445

&lt;211&gt; 405

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 445

Gly Thr Gly Leu Val Pro Ile Arg Gln Ser Thr Lys Phe Asp Ser Ser  
 1 5 10 15

Leu Asp Arg Lys Asp Lys Phe Ser Phe Asp Leu Gly Lys Gly Glu Val  
 20 25 30

Ile Lys Ala Trp Asp Ile Ala Ile Ala Thr Met Lys Val Gly Glu Val

393

35	40	45
Cys His Ile Thr Cys Lys Pro Glu Tyr Ala Tyr Gly Ser Ala Gly Ser		
50	55	60
Pro Pro Lys Ile Pro Pro Asn Ala Thr Leu Val Phe Glu Val Glu Leu		
65	70	75 80
Phe Glu Phe Lys Gly Glu Asp Leu Thr Glu Glu Glu Asp Gly Gly Ile		
	85	90 95
Ile Arg Arg Ile Gln Thr Arg Gly Glu Gly Tyr Ala Lys Pro Asn Glu		
	100	105 110
Gly Ala Ile Val Glu Val Ala Leu Glu Gly Tyr Tyr Lys Asp Lys Leu		
	115	120 125
Phe Asp Gln Arg Glu Leu Arg Phe Glu Ile Gly Glu Gly Glu Asn Leu		
	130	135 140
Asp Leu Pro Tyr Gly Leu Glu Arg Ala Ile Gln Arg Met Glu Lys Gly		
145	150	155 160
Glu His Ser Ile Val Tyr Leu Lys Pro Ser Tyr Ala Phe Gly Ser Val		
	165	170 175
Gly Lys Glu Lys Phe Gln Ile Pro Pro Asn Ala Glu Leu Lys Tyr Glu		
	180	185 190
Leu His Leu Lys Ser Phe Glu Lys Ala Lys Glu Ser Trp Glu Met Asn		
	195	200 205
Ser Glu Glu Lys Leu Glu Gln Ser Thr Ile Val Lys Glu Arg Gly Thr		
	210	215 220
Val Tyr Phe Lys Glu Gly Lys Tyr Lys Gln Ala Leu Leu Gln Tyr Lys		
225	230	235 240
Lys Ile Val Ser Trp Leu Glu Tyr Glu Ser Ser Phe Ser Asn Glu Glu		
	245	250 255
Ala Gln Lys Ala Gln Ala Leu Arg Leu Ala Ser His Leu Asn Leu Ala		
	260	265 270
Met Cys His Leu Lys Leu Gln Ala Phe Ser Ala Ala Ile Glu Ser Cys		
	275	280 285
Asn Lys Ala Leu Glu Leu Asp Ser Asn Asn Glu Lys Gly Leu Phe Arg		
	290	295 300
Arg Gly Glu Ala His Leu Ala Val Asn Asp Phe Glu Leu Ala Arg Ala		

394

```

305              310              315              320
Asp Phe Gln Lys Val Leu Gln Leu Tyr Pro Asn Asn Lys Ala Ala Lys
      325              330              335

Thr Gln Leu Ala Val Cys Gln Gln Arg Ile Arg Arg Gln Leu Ala Arg
      340              345              350

Glu Lys Lys Leu Tyr Ala Asn Met Phe Glu Arg Leu Ala Glu Glu Glu
      355              360              365

Asn Lys Ala Lys Ala Glu Ala Ser Ser Gly Asp His Pro Thr Asp Thr
      370              375              380

Glu Met Lys Glu Glu Gln Lys Ser Asn Thr Ala Gly Ser Gln Ser Gln
385              390              395              400

Val Glu Thr Glu Ala
      405

```

<210> 446  
 <211> 232  
 <212> PRT  
 <213> Homo sapiens

```

<400> 446
Pro Leu Val Pro Ser Ser Gln Lys Ala Leu Leu Leu Glu Leu Lys Gly
  1              5              10              15

Leu Gln Glu Glu Pro Val Glu Gly Phe Arg Val Thr Leu Val Asp Glu
      20              25              30

Gly Asp Leu Tyr Asn Trp Glu Val Ala Ile Phe Gly Pro Pro Asn Thr
      35              40              45

Tyr Tyr Glu Gly Gly Tyr Phe Lys Ala Arg Leu Lys Phe Pro Ile Asp
      50              55              60

Tyr Pro Tyr Ser Pro Pro Ala Phe Arg Phe Leu Thr Lys Met Trp His
      65              70              75              80

Pro Asn Ile Tyr Glu Thr Gly Asp Val Cys Ile Ser Ile Leu His Pro
      85              90              95

Pro Val Asp Asp Pro Gln Ser Gly Glu Leu Pro Ser Glu Arg Trp Asn
      100             105             110

Pro Thr Gln Asn Val Arg Thr Ile Leu Leu Ser Val Ile Ser Leu Leu
      115             120             125

```



395

Asn Glu Pro Asn Thr Phe Ser Pro Ala Asn Val Asp Ala Ser Val Met  
 130 135 140  
 Tyr Arg Lys Trp Lys Glu Ser Lys Gly Lys Asp Arg Glu Tyr Thr Asp  
 145 150 155 160  
 Ile Ile Arg Lys Gln Val Leu Gly Thr Arg Trp Thr Arg Val Asn Gly  
 165 170 175  
 Val Lys Val Pro Thr Thr Leu Ala Glu Tyr Cys Val Lys Thr Lys Ala  
 180 185 190  
 Pro Ala Pro Asp Glu Gly Ser Asp Leu Phe Tyr Asp Asp Tyr Tyr Glu  
 195 200 205  
 Asp Gly Glu Val Glu Glu Glu Ala Asp Ser Cys Phe Gly Asp Asp Glu  
 210 215 220  
 Asp Asp Ser Gly Thr Glu Glu Ser  
 225 230

&lt;210&gt; 447

&lt;211&gt; 356

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (12)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (53)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (191)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (263)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 447

Cys Ser Pro Pro Pro Pro Pro Ala Ala Ala Ala Xaa Ala Ala Ala Ala

396

1	5	10	15
Ala Met Ala Gln Tyr Lys Gly Ala Ala Ser Glu Ala Gly Arg Ala Met	20	25	30
His Leu Met Lys Lys Arg Glu Lys Gln Arg Glu Gln Met Glu Gln Met	35	40	45
Lys Gln Arg Ile Xaa Glu Glu Asn Ile Met Lys Ser Asn Ile Asp Lys	50	55	60
Lys Phe Ser Ala His Tyr Asp Ala Val Glu Ala Glu Leu Lys Ser Ser	65	70	75
Thr Val Gly Leu Val Thr Leu Asn Asp Met Lys Ala Lys Gln Glu Ala	85	90	95
Leu Val Lys Glu Arg Glu Lys Gln Leu Ala Lys Lys Glu Gln Ser Lys	100	105	110
Glu Leu Gln Met Lys Leu Glu Lys Leu Arg Glu Lys Glu Arg Lys Lys	115	120	125
Glu Ala Lys Arg Lys Ile Ser Ser Leu Ser Phe Thr Leu Glu Glu Glu	130	135	140
Glu Glu Gly Gly Glu Glu Glu Glu Glu Ala Ala Met Tyr Glu Glu Glu	145	150	155
Met Glu Arg Glu Glu Ile Thr Thr Lys Lys Arg Lys Leu Gly Lys Asn	165	170	175
Pro Asp Val Asp Thr Ser Phe Leu Pro Asp Arg Asp Arg Glu Xaa Glu	180	185	190
Glu Asn Arg Leu Arg Glu Glu Leu Arg Gln Glu Trp Glu Ala Lys Gln	195	200	205
Glu Lys Ile Lys Ser Glu Glu Ile Glu Ile Thr Phe Ser Tyr Trp Asp	210	215	220
Gly Ser Gly His Arg Arg Thr Val Lys Met Arg Lys Gly Asn Thr Met	225	230	235
Gln Gln Phe Leu Gln Lys Ala Leu Glu Ile Leu Arg Lys Asp Phe Ser	245	250	255
Glu Leu Arg Ser Ala Gly Xaa Glu Gln Leu Met Tyr Ile Lys Glu Asp	260	265	270
Leu Ile Ile Pro His His His Ser Phe Tyr Asp Phe Ile Val Thr Lys			

397

275                      280                      285  
 Ala Arg Gly Lys Ser Gly Pro Leu Phe Asn Phe Asp Val His Asp Asp  
 290                      295                      300  
 Val Arg Leu Leu Ser Asp Ala Thr Val Glu Lys Asp Glu Ser His Ala  
 305                      310                      315                      320  
 Gly Lys Val Val Leu Arg Ser Trp Tyr Glu Lys Asn Lys His Ile Phe  
 325                      330                      335  
 Pro Ala Ser Arg Trp Glu Pro Tyr Asp Pro Glu Lys Lys Trp Asp Lys  
 340                      345                      350  
 Tyr Thr Ile Arg  
 355

<210> 448  
 <211> 88  
 <212> PRT  
 <213> Homo sapiens

<400> 448  
 Lys Thr His Lys Met Cys Asp Ala Phe Val Gly Thr Trp Lys Leu Val  
 1                      5                      10                      15  
 Ser Ser Glu Asn Phe Asp Asp Tyr Met Lys Glu Val Gly Val Gly Phe  
 20                      25                      30  
 Ala Thr Arg Lys Val Ala Gly Met Ala Lys Pro Asn Met Ile Ile Ser  
 35                      40                      45  
 Val Asn Gly Asp Val Ile Thr Ile Lys Ser Glu Ser Thr Phe Lys Asn  
 50                      55                      60  
 Thr Glu Ile Ser Phe Ile Leu Gly Gln Glu Phe Asp Glu Ala Leu Gln  
 65                      70                      75                      80  
 Met Thr Gly Lys Ser Arg Ala Pro  
 85

<210> 449  
 <211> 171  
 <212> PRT  
 <213> Homo sapiens

<220>

398

&lt;221&gt; SITE

&lt;222&gt; (72)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (132)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 449

Leu Ile Leu Val Leu Met Phe Val Val Trp Met Lys Arg Arg Asp Lys  
 1 5 10 15

Glu Arg Gln Ala Lys Gln Leu Leu Ile Asp Pro Glu Asp Asp Val Arg  
 20 25 30

Asp Asn Ile Leu Lys Tyr Asp Glu Glu Gly Gly Gly Glu Glu Asp Gln  
 35 40 45

Asp Tyr Asp Leu Ser Gln Leu Gln Gln Pro Asp Thr Val Glu Pro Asp  
 50 55 60

Ala Ile Lys Pro Val Gly Ile Xaa Arg Met Asp Glu Arg Pro Ile His  
 65 70 75 80

Ala Glu Pro Gln Tyr Pro Val Arg Ser Ala Ala Pro His Pro Gly Asp  
 85 90 95

Ile Gly Asp Phe Ile Asn Glu Gly Leu Lys Ala Ala Asp Asn Asp Pro  
 100 105 110

Thr Ala Pro Pro Tyr Asp Ser Leu Leu Val Phe Asp Tyr Glu Gly Ser  
 115 120 125

Gly Ser Thr Xaa Gly Ser Leu Ser Ser Leu Asn Ser Ser Ser Ser Gly  
 130 135 140

Gly Glu Gln Asp Tyr Asp Tyr Leu Asn Asp Trp Gly Pro Arg Phe Lys  
 145 150 155 160

Lys Leu Ala Asp Met Tyr Gly Gly Gly Asp Asp  
 165 170

&lt;210&gt; 450

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 450

399

Lys Val Lys Ala Cys Cys Lys Asp Ile Phe Phe Leu Leu Leu Glu Gly  
 1 5 10 15  
 Asn Thr Lys Arg Lys Ile Ser Phe Phe His Gly Ala Phe Asp Asn Phe  
 20 25 30  
 Ser Leu

<210> 451  
 <211> 148  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (43)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (89)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 451  
 Arg Thr Leu His Pro Ala Thr Gly Pro Arg Ala Arg Pro Pro Arg Gly  
 1 5 10 15  
 Trp Arg Arg Arg Leu Cys Ala Gln Gly Pro Ala Pro Asp Trp Asp Pro  
 20 25 30  
 Gly Val Pro Pro Gly Leu Ala Ser Cys Gly Xaa Thr Val Trp Leu His  
 35 40 45  
 Phe Ser Asp Pro Ser Leu Gly Arg Lys Val Lys Glu Thr Gly Pro Ala  
 50 55 60  
 Ser Ala Phe Gly Leu Trp Phe Leu Asp Arg Val Leu Ser Pro Ser Pro  
 65 70 75 80  
 Pro Ser Ser Pro Asn Leu Ser His Xaa Arg Pro Leu Pro Ala Ala Pro  
 85 90 95  
 Ser Leu Leu Gly Ile Gly Ser Pro Glu Pro Pro Ser Pro Glu Pro Pro  
 100 105 110  
 Thr Pro Leu Pro Gly Pro Cys Gly Cys Trp Ala Ser His Leu Lys Glu  
 115 120 125

400

Gly Lys Val Val Gln Pro Glu Pro Val Glu Gln Cys Pro Val Trp Pro  
 130 135 140

Pro Lys Pro Lys  
 145

<210> 452  
 <211> 83  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (19)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (28)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (64)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (77)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (79)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 452  
 Asp Ser His Arg Pro Arg Ala Met Arg Ala Leu Trp Val Leu Gly Leu  
 1 5 10 15

Ser Cys Xaa Leu Leu Thr Phe Gly Ser Val Arg Xaa Asp Asp Glu Val  
 20 25 30

Asp Val Asp Gly Thr Val Glu Glu Asp Leu Gly Lys Ser Arg Glu Gly  
 35 40 45

Ser Arg Thr Asp Asp Glu Val Val Gln Arg Glu Glu Glu Ala Ile Xaa  
 50 55 60

401

Val Gly Trp Ile Lys Cys Ile Pro Asn Lys Arg Thr Xaa Glu Xaa Lys  
 65 70 75 80

Ser Arg Lys

<210> 453

<211> 240

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (234)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 453

Gly Trp Leu Pro Cys Gly Ser Ser Val Val Pro Ala Thr Pro Gly Ser  
 1 5 10 15

Pro Pro Ser Arg Phe Trp Leu Leu Pro Ala Met Ala Leu Arg Val Leu  
 20 25 30

Leu Leu Thr Ala Leu Thr Leu Cys His Gly Phe Asn Leu Asp Thr Glu  
 35 40 45

Asn Ala Met Thr Phe Gln Glu Asn Ala Arg Gly Phe Gly Gln Ser Val  
 50 55 60

Val Gln Leu Gln Gly Ser Arg Val Val Val Gly Ala Pro Gln Glu Ile  
 65 70 75 80

Val Ala Ala Asn Gln Arg Gly Ser Leu Tyr Gln Cys Asp Tyr Ser Thr  
 85 90 95

Gly Ser Cys Glu Pro Ile His Leu Gln Val Pro Val Glu Ala Val Asn  
 100 105 110

Met Ser Leu Gly Leu Ser Leu Ala Ala Thr Thr Ser Pro Pro Gln Leu  
 115 120 125

Leu Ala Cys Gly Pro Thr Val His Gln Thr Cys Ser Glu Asn Thr Tyr  
 130 135 140

Val Lys Gly Leu Cys Phe Leu Phe Gly Ser Asn Leu Arg Gln Gln Pro  
 145 150 155 160

Gln Lys Phe Pro Glu Ala Leu Arg Gly Cys Pro Gln Glu Asp Ser Asp  
 165 170 175

402

Ile Ala Phe Leu Ile Asp Gly Ser Gly Ser Ile Ile Pro His Asp Phe  
                   180                  185                  190

Arg Arg Met Lys Glu Phe Val Ser Thr Val Met Glu Gln Leu Lys Lys  
                   195                  200                  205

Ser Lys Thr Leu Phe Ser Leu Met Gln Tyr Ser Glu Glu Phe Arg Ile  
                   210                  215                  220

His Phe Thr Ser Lys Ser Ser Arg Thr Xaa Leu Thr Gln Asp His Trp  
                   225                  230                  235                  240

&lt;210&gt; 454

&lt;211&gt; 244

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (206)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (227)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (229)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (239)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 454

Lys Trp Cys Ser Trp Thr Leu Leu Lys Ile Trp Glu Val Thr Cys Thr  
           1                  5                  10                  15

Trp Lys Leu Pro Thr Leu Ala Lys Phe Ser Pro Tyr Leu Gly Gln Met  
                   20                  25                  30

Ile Asn Leu Arg Arg Leu Leu Leu Ser His Ile His Ala Ser Ser Tyr



403

35                      40                      45  
 Ile Ser Pro Glu Lys Glu Glu Gln Tyr Ile Ala Gln Phe Thr Ser Gln  
     50                      55                      60  
 Phe Leu Ser Leu Gln Cys Leu Gln Leu Leu Tyr Val Asp Ser Leu Phe  
     65                      70                      75                      80  
 Phe Leu Arg Gly Arg Leu Asp Gln Leu Leu Arg His Val Met Asn Pro  
                     85                      90                      95  
 Leu Glu Thr Leu Ser Ile Thr Asn Cys Arg Leu Ser Glu Gly Asp Val  
                     100                      105                      110  
 Met His Leu Ser Gln Ser Pro Ser Val Ser Gln Leu Ser Val Leu Ser  
                     115                      120                      125  
 Leu Ser Gly Val Met Leu Thr Asp Val Ser Pro Glu Pro Leu Gln Ala  
                     130                      135                      140  
 Leu Leu Glu Arg Ala Ser Ala Thr Leu Gln Asp Leu Val Phe Asp Glu  
     145                      150                      155                      160  
 Cys Gly Ile Thr Asp Asp Gln Leu Leu Ala Leu Leu Pro Ser Leu Ser  
                     165                      170                      175  
 His Cys Ser Gln Leu Thr Thr Leu Ser Phe Tyr Gly Asn Ser Ile Ser  
                     180                      185                      190  
 Ile Ser Ala Leu Gln Ser Leu Leu Gln His Leu Ile Gly Xaa Ser Asn  
                     195                      200                      205  
 Leu Thr His Val Leu Tyr Pro Val Pro Leu Glu Ser Tyr Glu Asp Ile  
                     210                      215                      220  
 His Gly Xaa Leu Xaa Leu Glu Arg Leu Leu Ser Ala Cys Gln Xaa Gln  
     225                      230                      235                      240  
 Gly Val Ala Val

&lt;210&gt; 455

&lt;211&gt; 195

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 455

His Glu Gly Thr Gln Ser Phe Val Phe Gln Arg Glu Glu Ile Ala Gln  
     1                      5                      10                      15

404

Leu Ala Arg Gln Tyr Ala Gly Leu Asp His Glu Leu Ala Phe Ser Arg  
                   20                                  25                                  30  
 Leu Ile Val Glu Leu Arg Arg Leu His Pro Gly His Val Leu Pro Asp  
                   35                                  40                                  45  
 Glu Glu Leu Gln Trp Val Phe Val Asn Ala Gly Gly Trp Met Gly Ala  
                   50                                  55                                  60  
 Met Cys Leu Leu His Ala Ser Leu Ser Glu Tyr Val Leu Leu Phe Gly  
                   65                                  70                                  75                                  80  
 Thr Ala Leu Gly Ser Arg Gly His Ser Gly Arg Tyr Trp Ala Glu Ile  
                                   85                                  90                                  95  
 Ser Asp Thr Ile Ile Ser Gly Thr Phe His Gln Trp Arg Glu Gly Thr  
                   100                                  105                                  110  
 Thr Lys Ser Glu Val Phe Tyr Pro Gly Glu Thr Val Val His Gly Pro  
                   115                                  120                                  125  
 Gly Glu Ala Thr Ala Val Glu Trp Gly Pro Asn Thr Trp Met Val Glu  
                   130                                  135                                  140  
 Tyr Gly Arg Gly Val Ile Pro Ser Thr Leu Ala Phe Ala Leu Ala Asp  
                   145                                  150                                  155                                  160  
 Thr Val Phe Ser Thr Gln Asp Phe Leu Thr Leu Phe Tyr Thr Leu Arg  
                                   165                                  170                                  175  
 Ser Tyr Ala Arg Gly Leu Arg Leu Glu Leu Thr Thr Tyr Leu Phe Gly  
                   180                                  185                                  190  
 Gln Asp Pro  
                   195

&lt;210&gt; 456

&lt;211&gt; 36

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 456

Leu Val Thr Leu Leu His Ala Met Gln Ala Arg Asp Lys Thr Leu Gly  
           1                                  5                                  10                                  15  
 Leu Ala Thr Leu Cys Ile Gly Gly Gly Gln Gly Ile Ala Met Val Ile  
                   20                                  25                                  30

405

Glu Arg Leu Asn

35

&lt;210&gt; 457

&lt;211&gt; 152

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (86)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (114)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 457

Val Thr Ala Ala Ala Ser Val Arg Ala Leu Gln Val Thr Val Ala Gly

1

5

10

15

Leu Leu Leu Val Phe Phe Leu Phe Gly Ala Pro Leu Asp Ser Leu Pro

20

25

30

Ser Met Lys Ala Leu Ser Pro Val Arg Gly Cys Tyr Glu Ala Val Cys

35

40

45

Cys Leu Ser Glu Arg Ser Leu Ala Ile Ala Arg Gly Arg Gly Lys Gly

50

55

60

Pro Ala Ala Glu Glu Pro Leu Ser Leu Leu Asp Asp Met Asn His Cys

65

70

75

80

Tyr Ser Arg Leu Arg Xaa Leu Val Pro Gly Val Pro Arg Gly Thr Gln

85

90

95

Leu Ser Gln Val Glu Ile Leu Gln Arg Val Ile Asp Tyr Ile Leu Asp

100

105

110

Leu Xaa Val Val Leu Ala Glu Pro Ala Pro Gly Pro Pro Asp Gly Pro

115

120

125

His Leu Pro Ile Gln Thr Ala Glu Leu Ala Pro Glu Leu Val Ile Ser

130

135

140

Asn Asp Lys Arg Ser Phe Cys His

145

150

<210> 458  
 <211> 31  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (17)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (25)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (31)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 458  
 Leu Leu Asn Asn Phe Ile Phe Leu Glu Thr His Tyr Leu Trp Ala Cys  
       1                  5                  10                  15  
 Xaa Thr Trp Thr Ile Trp Pro Asn Xaa Leu Asp Lys Lys Gly Xaa  
                   20                  25                  30

<210> 459  
 <211> 157  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (28)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (72)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (124)  
 <223> Xaa equals any of the naturally occurring L-amino acids

407

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (130)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 459

Asp Pro Arg Val Arg Glu Thr Thr Val Lys Ala Arg Ala Arg Ser Gln  
 1 5 10 15

His Ala Gly Gly Pro Glu Leu Gly Leu Ser Gln Xaa Tyr Val Thr Pro  
 20 25 30

Arg Arg Pro Phe Glu Lys Ser Arg Leu Asp Gln Glu Leu Lys Leu Ile  
 35 40 45

Gly Glu Tyr Gly Leu Arg Asn Lys Arg Glu Val Trp Arg Val Lys Phe  
 50 55 60

Thr Leu Ala Lys Ile Arg Lys Xaa Ala Arg Glu Leu Leu Thr Leu Asp  
 65 70 75 80

Glu Lys Asp Pro Arg Arg Leu Phe Glu Gly Asn Ala Leu Leu Arg Arg  
 85 90 95

Leu Val Arg Ile Gly Val Leu Asp Glu Gly Lys Met Lys Leu Asp Tyr  
 100 105 110

Ile Leu Gly Leu Lys Met Arg Ile Leu Gly Glu Xaa Ser Ala Asp Pro  
 115 120 125

Gly Xaa Ser Ser Trp Gly Trp Pro Ile His Pro Pro Cys Pro Val Leu  
 130 135 140

Ile Arg Gln Ala Thr Gln Val Arg Lys Gln Val Val Asn  
 145 150 155

&lt;210&gt; 460

&lt;211&gt; 136

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (119)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (130)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (135)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 460

Ile Trp Ala Pro Phe Pro His His Gln Gly Ser Gly Ser Gln Val Ser  
1 5 10 15

Ser Tyr Gly Thr Gly Ala Leu Lys Ser His Ile Met Ala Ala Lys Ala  
20 25 30

Val Ala Asn Thr Met Arg Thr Ser Leu Gly Pro Asn Gly Leu Asp Lys  
35 40 45

Met Met Val Asp Lys Asp Gly Asp Val Thr Val Thr Asn Asp Gly Ala  
50 55 60

Thr Ile Leu Ser Met Met Asp Val Asp His Gln Ile Ala Lys Leu Met  
65 70 75 80

Val Glu Leu Ser Lys Ser Gln Asp Asp Glu Ile Gly Asp Gly Asp His  
85 90 95

Gly Gly Gly Cys Pro Gly Arg Arg Pro Ala Gly Arg Arg Pro Ser Ser  
100 105 110

Cys Trp Thr Ala Ala Phe Xaa Arg Ser Gly Ser Pro Thr Val Thr Ser  
115 120 125

Arg Xaa Pro Ala Leu Ala Xaa Glu  
130 135

<210> 461

<211> 390

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (11)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (14)

<223> Xaa equals any of the naturally occurring L-amino acids

409

<220>  
 <221> SITE  
 <222> (375)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (382)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (383)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (386)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (387)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 461  
 Cys Gly Asn Trp Trp Val Pro Arg Ala Gly Xaa Asn Trp Xaa Arg Gly  
   1                  5                  10                  15  
 Ser Arg Phe Leu Phe Val Asp Arg Cys Asp Arg His Leu Thr Met Gln  
           20                  25                  30  
 Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu  
       35                  40                  45  
 Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu  
       50                  55                  60  
 Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu  
   65                  70                  75                  80  
 Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr  
           85                  90                  95  
 Leu His Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys  
       100                  105                  110  
 Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr  
       115                  120                  125

410

```

Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro
 130                      135                      140

Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg
145                      150                      155                      160

Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val
                      165                      170                      175

Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu Thr Gly
                      180                      185                      190

Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val
195                      200                      205

Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg
210                      215                      220

Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp
225                      230                      235                      240

Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg
                      245                      250                      255

Gly Gly Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr
260                      265                      270

Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile
275                      280                      285

Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala
290                      295                      300

Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln
305                      310                      315                      320

Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Met Gln
                      325                      330                      335

Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu
340                      345                      350

Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Arg Ser Arg Gln Gly Arg
355                      360                      365

His Pro Pro Asp Gln Gln Xaa Leu Ile Leu Leu Gly Lys Xaa Xaa Lys
370                      375                      380

Trp Xaa Xaa Pro Phe Asp
385                      390

```



411

&lt;210&gt; 462

&lt;211&gt; 171

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (74)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (135)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (142)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (155)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 462

Cys	Ser	Thr	Val	Arg	Ile	Pro	Gly	Ser	Thr	His	Ala	Ser	Gly	Leu	Ser
1				5					10					15	

Arg	Arg	Ala	Ser	Pro	Val	Tyr	Leu	Ala	Ser	Met	Ser	Gly	Arg	Gly	Lys
		20						25					30		

Thr	Gly	Gly	Lys	Ala	Arg	Ala	Lys	Ala	Lys	Ser	Arg	Ser	Ser	Arg	Ala
		35					40					45			

Gly	Leu	Gln	Phe	Pro	Val	Gly	Arg	Val	His	Arg	Leu	Leu	Arg	Lys	Gly
	50					55					60				

His	Tyr	Ala	Glu	Arg	Val	Gly	Ala	Gly	Xaa	Pro	Val	Tyr	Leu	Ala	Ala
65				70						75				80	

Val	Leu	Glu	Tyr	Leu	Thr	Ala	Glu	Ile	Leu	Glu	Leu	Ala	Gly	Asn	Ala
			85						90					95	

Ala	Arg	Asp	Asn	Lys	Lys	Thr	Arg	Ile	Ile	Pro	Arg	His	Leu	Gln	Leu
		100						105					110		

Ala	Ile	Arg	Asn	Asp	Glu	Glu	Leu	Asn	Lys	Leu	Leu	Gly	Gly	Val	Thr
		115					120					125			

412

Ile Ala Gln Gly Arg Arg Xaa Ala Gln His Pro Gly Arg Xaa Cys Cys  
 130 135 140

Pro Arg Arg Pro Ala Pro Pro Trp Gly Arg Xaa Pro Phe Gly Gly Gln  
 145 150 155 160

Glu Arg Ala Thr Lys Ala Ser Gln Gly Val Leu  
 165 170

&lt;210&gt; 463

&lt;211&gt; 433

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 463

Arg Val Arg Ala Pro Pro Arg Pro Pro Leu Gly Pro Ser Arg Pro Ser  
 1 5 10 15

His His Val His Pro Leu Gln Leu Pro Gly Ile Arg Glu Val Thr Ile  
 20 25 30

Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala Asp Pro Ser Leu  
 35 40 45

Gln Arg Val Arg Gln Glu Glu Ser Glu Gln Ile Lys Thr Leu Asn Asn  
 50 55 60

Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu Glu Gln Gln Asn  
 65 70 75 80

Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu Gln Lys Ser Ala  
 85 90 95

Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln Ile Ala Gly Leu  
 100 105 110

Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly Arg Leu Glu Ala  
 115 120 125

Glu Leu Arg Ser Met Gln Asp Val Val Glu Asp Phe Lys Asn Lys Tyr  
 130 135 140

Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn Glu Phe Val Val  
 145 150 155 160

Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys Val Glu Leu Glu  
 165 170 175

413

Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe Leu Arg Thr Leu  
 180 185 190  
 Asn Glu Thr Glu Leu Thr Glu Leu Gln Ser Gln Ile Ser Asp Thr Ser  
 195 200 205  
 Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp Leu Asp Gly Ile  
 210 215 220  
 Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala Lys Cys Ser Arg  
 225 230 235 240  
 Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu Thr Leu Gln Ala  
 245 250 255  
 Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr Arg Asn Glu Ile  
 260 265 270  
 Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala Glu Ile Asp Asn  
 275 280 285  
 Ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala Ile Ala Glu Ala Glu  
 290 295 300  
 Glu Arg Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala Lys Gln Glu Glu  
 305 310 315 320  
 Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met Ala Arg Gln Leu  
 325 330 335  
 Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala Leu Asp Ile Glu  
 340 345 350  
 Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser Arg Leu Ala  
 355 360 365  
 Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met Asn Ser Thr Gly  
 370 375 380  
 Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu Gly Gly Thr Met  
 385 390 395 400  
 Gly Ser Asn Ala Leu Ser Phe Ser Ser Ser Ala Gly Pro Gly Leu Leu  
 405 410 415  
 Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg Arg Ser Ala Arg  
 420 425 430

Asp

<210> 464  
 <211> 121  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (50)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (64)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (110)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (114)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (115)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (117)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 464  
 Gly Ser Gly Cys Val Phe Ala Ile Leu Gly Arg Arg Cys Ser Arg Pro  
     1                    5                    10                    15  
 Trp Arg Ile Trp Pro Gly Glu Pro Leu Gln Arg Ala Pro Pro Ala Ala  
                     20                    25                    30  
 Gly Thr Arg Trp Pro His Gly His Arg Ser Ser Pro Val Gly Thr Pro  
             35                    40                    45  
 Gly Xaa Ala Pro Asn Val Pro Ala Ile Trp Gln Gln Pro Leu Trp Xaa  
     50                    55                    60  
 Glu Tyr Ser Cys Glu Tyr Gly Ser Met Lys Phe Tyr Ala Leu Cys Gly

65					70					75					80	
Phe	Gly	Gly	Val	Leu	Ser	Cys	Gly	Leu	Thr	His	Thr	Ala	Val	Val	Pro	
				85					90					95		
Leu	Asp	Leu	Val	Lys	Cys	Arg	Met	Gln	Val	Asp	Pro	Gln	Xaa	Tyr	Lys	
				100					105					110		
Gly	Xaa	Xaa	Asn	Xaa	Ile	Leu	Ile	Asn								
				115					120							

```
<210> 465
<211> 68
<212> PRT
<213> Homo sapiens
```

```

<400> 465
Arg Ile Pro Ala Pro Ala Ser Ser Arg His Ser Gly Gly Arg Cys Ala
 1                5                10                15
Ala Gly Pro Arg Gly Pro Pro Ala Thr Ala Ser Arg Ala Leu Arg Ala
 20                25                30
Val His Arg Pro Leu Asp Ala Ala Arg Gly Arg Thr Gly Ser Thr Ser
 35                40                45
His Leu Cys Ser Ser Ser Tyr Thr Ile Gly Cys Leu Leu Trp Phe Ser
 50                55                60
Gln Lys Ala Met
65

```

```
<210> 466
<211> 224
<212> PRT
<213> Homo sapiens
```

```

<400> 466
Ala Thr Ile Leu Glu Arg Glu Ala Glu Gln Ser Arg Leu Gly Ala Thr
 1               5               10              15
Glu Arg Ala Ala Ala Ala Met Asn Pro Glu Tyr Asp Tyr Leu Phe
      20              25              30
Lys Leu Leu Leu Ile Gly Asp Ser Gly Val Gly Lys Ser Cys Leu Leu
 35              40              45

```

416

Leu Arg Phe Ala Asp Asp Thr Tyr Thr Glu Ser Tyr Ile Ser Thr Ile  
 50 55 60  
 Gly Val Asp Phe Lys Ile Arg Thr Ile Glu Leu Asp Gly Lys Thr Ile  
 65 70 75 80  
 Lys Leu Gln Ile Trp Asp Thr Ala Gly Gln Glu Arg Phe Arg Thr Ile  
 85 90 95  
 Thr Ser Ser Tyr Tyr Arg Gly Ala His Gly Ile Ile Val Val Tyr Asp  
 100 105 110  
 Val Thr Asp Gln Glu Ser Tyr Ala Asn Val Lys Gln Trp Leu Gln Glu  
 115 120 125  
 Ile Asp Arg Tyr Ala Ser Glu Asn Val Asn Lys Leu Leu Val Gly Asn  
 130 135 140  
 Lys Ser Asp Leu Thr Thr Lys Lys Val Val Asp Asn Thr Thr Ala Lys  
 145 150 155 160  
 Glu Phe Ala Asp Ser Leu Gly Ile Pro Phe Leu Glu Thr Ser Ala Lys  
 165 170 175  
 Asn Ala Thr Asn Val Glu Gln Ala Phe Met Thr Met Ala Ala Glu Ile  
 180 185 190  
 Lys Lys Arg Met Gly Pro Gly Ala Ala Ser Gly Gly Glu Arg Pro Asn  
 195 200 205  
 Leu Lys Ile Asp Ser Thr Pro Val Lys Pro Ala Gly Gly Gly Cys Cys  
 210 215 220

&lt;210&gt; 467

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 467

Ser Glu Ala Pro Gly Glu Ser Val Gly Thr Thr Pro Glu Ala Gln Met  
 1 5 10 15

Lys Thr Gly Pro Phe Ala Glu His Ser Asn Gln Leu Trp Asn Ile Ser  
 20 25 30

Ala Val Pro Ser Trp Ser Lys Val Asn Gln Gly Leu Ile Arg Met Tyr

417

35                      40                      45  
 Lys Ala Glu Cys Leu Glu Lys Phe Pro Val Ile Gln His Phe Lys Phe  
 50                      55                      60  
 Gly Ser Leu Leu Pro Ile His Pro Val Thr Ser Gly  
 65                      70                      75

<210> 468  
 <211> 111  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (31)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (35)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (47)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (49)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (78)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (97)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 468  
 Ser Leu Ala Arg Thr Gly Pro Arg Ser Leu Ala Arg Pro Cys Arg Arg  
 1                      5                      10                      15

Arg Pro Ala His Arg His Pro Leu Gln Pro Cys Pro Pro Gly Xaa Cys  
 20                      25                      30

```
<210> 469
<211> 459
<212> PRT
<213> Homo sapiens
```

```

<400> 469
Pro Arg Val Arg Pro Arg Val Arg Pro Arg Val Arg Leu Ser Ser Pro
  1             5             10             15

Ser Pro Val Cys Leu Pro Pro Ala Ala Ala Thr Met Thr Thr Ser Ile
          20             25             30

Arg Gln Phe Thr Ser Ser Ser Ser Ile Lys Gly Ser Ser Gly Leu Gly
      35             40             45

Gly Gly Ser Ser Arg Thr Ser Cys Arg Leu Ser Gly Gly Leu Gly Ala
      50             55             60

Gly Ser Cys Arg Leu Gly Ser Ala Gly Gly Leu Gly Ser Thr Leu Gly
      65             70             75             80

Gly Ser Ser Tyr Ser Ser Cys Tyr Ser Phe Gly Ser Gly Gly Gly Tyr
          85             90             95

Gly Ser Ser Phe Gly Gly Val Asp Gly Leu Leu Ala Gly Gly Glu Lys
          100             105             110

Ala Thr Met Gln Asn Leu Asn Asp Arg Leu Ala Ser Tyr Leu Asp Lys
      115             120             125

Val Arg Ala Leu Glu Glu Ala Asn Thr Glu Leu Glu Val Lys Ile Arg
      130             135             140

```



Asp Trp Tyr Gln Arg Gln Ala Pro Gly Pro Ala Arg Asp Tyr Ser Gln  
 145 150 155 160  
 Tyr Tyr Arg Thr Ile Glu Glu Leu Gln Asn Lys Ile Leu Thr Ala Thr  
 165 170 175  
 Val Asp Asn Ala Asn Ile Leu Leu Gln Ile Asp Asn Ala Arg Leu Ala  
 180 185 190  
 Ala Asp Asp Phe Arg Thr Lys Phe Glu Thr Glu Gln Ala Leu Arg Leu  
 195 200 205  
 Ser Val Glu Ala Asp Ile Asn Gly Leu Arg Arg Val Leu Asp Glu Leu  
 210 215 220  
 Thr Leu Ala Arg Ala Asp Leu Glu Met Gln Ile Glu Asn Leu Lys Glu  
 225 230 235 240  
 Glu Leu Ala Tyr Leu Lys Lys Asn His Glu Glu Glu Met Asn Ala Leu  
 245 250 255  
 Arg Gly Gln Val Gly Gly Glu Ile Asn Val Glu Met Asp Ala Ala Pro  
 260 265 270  
 Gly Val Asp Leu Ser Arg Ile Leu Asn Glu Met Arg Asp Gln Tyr Glu  
 275 280 285  
 Lys Met Ala Glu Lys Asn Arg Lys Asp Ala Glu Asp Trp Phe Phe Ser  
 290 295 300  
 Lys Thr Glu Glu Leu Asn Arg Glu Val Ala Thr Asn Ser Glu Leu Val  
 305 310 315 320  
 Gln Ser Gly Lys Ser Glu Ile Ser Glu Leu Arg Arg Thr Met Gln Ala  
 325 330 335  
 Leu Glu Ile Glu Leu Gln Ser Gln Leu Ser Met Lys Ala Ser Leu Glu  
 340 345 350  
 Gly Asn Leu Ala Glu Thr Glu Asn Arg Tyr Cys Val Gln Leu Ser Gln  
 355 360 365  
 Ile Gln Gly Leu Ile Gly Ser Val Glu Glu Gln Leu Ala Gln Leu Arg  
 370 375 380  
 Cys Glu Met Glu Gln Gln Asn Gln Glu Tyr Lys Ile Leu Leu Asp Val  
 385 390 395 400  
 Lys Thr Arg Leu Glu Gln Glu Ile Ala Thr Tyr Arg Arg Leu Leu Glu  
 405 410 415

420

Gly Glu Asp Ala His Leu Thr Gln Tyr Lys Lys Glu Pro Val Thr Thr  
                   420                  425                  430

Arg Gln Val Arg Thr Ile Val Glu Glu Val Gln Asp Gly Lys Val Ile  
                   435                  440                  445

Ser Ser Arg Glu Gln Val His Gln Thr Thr Arg  
           450                  455

&lt;210&gt; 470

&lt;211&gt; 158

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (158)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 470

Pro Pro Pro Pro Pro Pro Pro Glu Leu Cys Ser Met Ala Ser Arg Arg  
   1                  5                  10                  15

Met Glu Thr Lys Pro Val Ile Thr Cys Leu Lys Thr Leu Leu Ile Ile  
                   20                  25                  30

Tyr Ser Phe Val Phe Trp Ile Thr Gly Val Ile Leu Leu Ala Val Gly  
                   35                  40                  45

Val Trp Gly Lys Leu Thr Leu Gly Thr Tyr Ile Ser Leu Ile Ala Glu  
                   50                  55                  60

Asn Ser Thr Asn Ala Pro Tyr Val Leu Ile Gly Thr Gly Thr Thr Ile  
   65                  70                  75                  80

Val Val Phe Gly Leu Phe Gly Cys Phe Ala Thr Cys Arg Gly Ser Pro  
                   85                  90                  95

Trp Met Leu Lys Leu Tyr Ala Met Phe Leu Ser Leu Val Phe Leu Ala  
                   100                  105                  110

Glu Leu Val Ala Gly Ile Ser Gly Phe Val Phe Arg His Glu Ile Lys  
                   115                  120                  125

Asp Thr Phe Leu Arg Thr Tyr Thr Asp Ala Met Gln Thr Tyr Asn Gly  
                   130                  135                  140

Asn Asp Glu Arg Ser Arg Ala Val Asp His Val Gln Arg Xaa  
   145                  150                  155

421

&lt;210&gt; 471

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

Val Leu Phe Phe Tyr Glu Cys Pro Asn Leu Cys Phe Pro Leu Pro Ser  
1 5 10 15

Gln Thr Val Trp Pro Val Glu Ser Val Trp Phe Val Phe Ile Ser Pro  
20 25 30

Ser Phe Leu Glu Gln Gly Leu Arg Pro Cys His Ile Ser Tyr Ala Leu  
35 40 45

His Pro Arg Leu Phe Trp Thr Leu Lys Val Asp  
50 55

&lt;210&gt; 472

&lt;211&gt; 320

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (48)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (49)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (53)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (105)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 472

Asp Pro Asp Glu Val Phe Pro Val Cys Leu Pro Leu Thr Gly Asp Ala  
1 5 10 15

422

Gly Glu Asp Gly Gly Lys Met Leu His Leu Pro Glu Trp Pro Glu Gln  
 20 25 30  
 Pro Pro Gly Gly Pro Ala Ala Leu Gln Val Arg Gly Ala Glu Asp Xaa  
 35 40 45  
 Xaa Leu Ser Phe Xaa Asp Cys Glu Ser Leu Gln Ala Val Phe Asp Pro  
 50 55 60  
 Ala Ser Cys Pro His Met Leu Arg Ala Pro Ala Arg Val Leu Gly Glu  
 65 70 75 80  
 Ala Val Leu Pro Phe Ser Pro Ala Leu Ala Glu Val Thr Leu Gly Ile  
 85 90 95  
 Gly Arg Gly Ala Gly Ser Ser Trp Xaa Tyr His Glu Glu Glu Ala Asp  
 100 105 110  
 Ser Thr Ala Lys Ala Met Val Thr Glu Met Cys Leu Gly Glu Glu Asp  
 115 120 125  
 Phe Gln Gln Leu Gln Ala Gln Glu Gly Val Ala Ile Thr Phe Cys Leu  
 130 135 140  
 Lys Glu Phe Arg Gly Leu Leu Ser Phe Ala Glu Ser Ala Asn Leu Asn  
 145 150 155 160  
 Leu Ser Ile His Phe Asp Ala Pro Gly Arg Pro Ala Ile Phe Thr Ile  
 165 170 175  
 Lys Asp Ser Leu Leu Asp Gly His Phe Val Leu Ala Thr Leu Ser Asp  
 180 185 190  
 Thr Asp Ser His Ser Gln Asp Leu Gly Ser Pro Glu Arg His Gln Pro  
 195 200 205  
 Val Pro Gln Leu Gln Ala His Ser Thr Pro His Pro Asp Asp Phe Ala  
 210 215 220  
 Asn Asp Asp Ile Asp Ser Tyr Met Ile Ala Met Glu Thr Thr Ile Gly  
 225 230 235 240  
 Asn Glu Gly Ser Arg Val Leu Pro Ser Ile Ser Leu Ser Pro Gly Pro  
 245 250 255  
 Gln Pro Pro Lys Ser Pro Gly Pro His Ser Glu Glu Glu Asp Glu Ala  
 260 265 270  
 Glu Pro Ser Thr Val Pro Gly Thr Pro Pro Pro Lys Lys Phe Arg Ser  
 275 280 285

423

Leu Phe Phe Gly Ser Ile Leu Ala Pro Val Arg Ser Pro Gln Gly Pro  
 290 295 300

Ser Leu Cys Trp Arg Lys Thr Val Arg Val Lys Ala Glu Pro Arg Thr  
 305 310 315 320

&lt;210&gt; 473

&lt;211&gt; 331

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (24)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (283)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (299)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (324)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 473

Pro Pro Cys Ala Val Pro Gly Pro Arg Leu Ser Pro Lys Leu Arg Thr  
 1 5 10 15

Pro Ser Asn Ser Arg Glu Ser Xaa Ile Cys Val Ser Gly Arg Ala Glu  
 20 25 30

Ala Leu Thr Phe Arg His Gly Ala Glu Gly Ser Asp Arg Arg Gln  
 35 40 45

Arg Arg Glu Gly Val Leu Gly Pro Ala Leu Leu Cys Arg Pro Trp Glu  
 50 55 60

Val Leu Gly Ala His Glu Val Pro Ser Arg Asn Ile Phe Ser Glu Gln

424

65		70		75		80									
Thr	Ile	Pro	Pro	Ser	Ala	Lys	Tyr	Gly	Gly	Arg	His	Thr	Val	Thr	Met
				85					90					95	
Ile	Pro	Gly	Asp	Gly	Ile	Gly	Pro	Glu	Leu	Met	Leu	His	Val	Lys	Ser
			100					105					110		
Val	Phe	Arg	His	Ala	Cys	Val	Pro	Val	Asp	Phe	Glu	Glu	Val	His	Val
			115				120					125			
Ser	Ser	Asn	Ala	Asp	Glu	Glu	Asp	Ile	Arg	Asn	Ala	Ile	Met	Ala	Ile
		130					135				140				
Arg	Arg	Asn	Arg	Val	Ala	Leu	Lys	Gly	Asn	Ile	Glu	Thr	Asn	His	Asn
145					150				155						160
Leu	Pro	Pro	Ser	His	Lys	Ser	Arg	Asn	Asn	Ile	Leu	Arg	Thr	Ser	Leu
				165					170					175	
Asp	Leu	Tyr	Ala	Asn	Val	Ile	His	Cys	Lys	Ser	Leu	Pro	Gly	Val	Val
			180					185					190		
Thr	Arg	His	Lys	Asp	Ile	Asp	Ile	Leu	Ile	Val	Arg	Glu	Asn	Thr	Glu
		195					200					205			
Gly	Glu	Tyr	Ser	Ser	Leu	Glu	His	Glu	Ser	Val	Ala	Gly	Val	Val	Glu
		210					215				220				
Ser	Leu	Lys	Ile	Ile	Thr	Lys	Ala	Lys	Ser	Leu	Arg	Ile	Ala	Glu	Tyr
225					230					235				240	
Ala	Phe	Lys	Leu	Ala	Gln	Glu	Ser	Gly	Arg	Lys	Lys	Val	Thr	Ala	Val
				245					250					255	
His	Lys	Ala	Asn	Ile	Met	Lys	Leu	Gly	Asp	Gly	Leu	Phe	Leu	Gln	Cys
			260					265					270		
Cys	Arg	Glu	Val	Ala	Ala	Arg	Tyr	Pro	Gln	Xaa	Thr	Phe	Glu	Asn	Met
		275					280					285			
Ile	Val	Asp	Asn	Thr	Thr	Met	Gln	Leu	Val	Xaa	Arg	Pro	Gln	Gln	Phe
		290				295					300				
Asp	Val	Met	Val	Met	Pro	Asn	Leu	Tyr	Gly	Asn	Ile	Val	Lys	Gln	Cys
305					310					315				320	
Leu	Arg	Gly	Xaa	Gly	Arg	Gly	Pro	Lys	Leu	Val					
				325					330						

425

&lt;210&gt; 474

&lt;211&gt; 30

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

Thr Pro Ile Ser Thr Lys Asn Thr Lys Ile Ser Gln Ala Arg Trp Arg  
 1 5 10 15

Ala His Val Val Pro Ala Thr Arg Glu Ala Asp Ala Glu Glu  
 20 25 30

&lt;210&gt; 475

&lt;211&gt; 124

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (110)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 475

Thr Gln Phe Ser Leu Ser Pro Val Glu Thr Ile Tyr Thr Ile Leu Cys  
 1 5 10 15

Ile Asn Val Tyr Thr Leu Pro Ile Cys Ile His Ile Tyr Ile Val Tyr  
 20 25 30

Ile Leu Tyr Met Tyr Arg Cys Val Tyr Val His Ile Tyr Thr His Ala  
 35 40 45

His Asn Lys Ile Arg Cys Ser Leu Gln Ile Gln Met Leu Ile Thr Lys  
 50 55 60

Pro Asp Ala Thr Gln Thr Ala Ala Glu Glu Thr Arg Leu Asp Ser Cys  
 65 70 75 80

Asn Arg Ser Gln Lys Ile Lys Thr Ala Thr Cys Ser Asp Phe Gly His  
 85 90 95

Phe Cys Met Phe Ile Lys Asn Gly Phe Val Thr Arg Lys Xaa Arg Thr  
 100 105 110

Ser Val Ser Glu Lys Gly Arg Trp Gly Glu Pro Ser  
 115 120

426

&lt;210&gt; 476

&lt;211&gt; 64

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 476

Asn Gly Tyr Leu Val Phe Pro Arg Lys Asn Ser Phe Leu Leu Ile Phe  
 1 5 10 15

Gly Leu Phe Val Tyr Leu Glu Thr Asn Leu Asp Ser Leu Pro Leu Val  
 20 25 30

Asp Thr His Ser Lys Arg Thr Leu Leu Ile Lys Thr Val Glu Thr Arg  
 35 40 45

Asp Gly Gln Val Ile Asn Glu Thr Ser Gln His His Asp Asp Leu Glu  
 50 55 60

&lt;210&gt; 477

&lt;211&gt; 107

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 477

Val Leu Thr Val Asp Ala Arg Asn His Gly Asp Ser Pro His Ser Pro  
 1 5 10 15

Asp Met Ser Tyr Glu Ile Met Ser Gln Asp Leu Gln Asp Leu Leu Pro  
 20 25 30

Gln Leu Gly Leu Val Pro Cys Val Val Val Gly His Ser Met Gly Gly  
 35 40 45

Lys Thr Ala Met Leu Leu Ala Leu Gln Arg Pro Glu Leu Val Glu Arg  
 50 55 60

Leu Ile Ala Val Asp Ile Ser Pro Val Glu Ser Thr Gly Val Ser His  
 65 70 75 80

Phe Ala Thr Tyr Val Ala Ala Met Arg Ala Ile Asn Ile Ala Asp Arg  
 85 90 95

Leu Ala Pro Leu Pro Cys Pro Lys Thr Gly Gly  
 100 105



427

&lt;210&gt; 478

&lt;211&gt; 282

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (281)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 478

Arg Glu Leu Gly Gly Thr Leu Leu Ser Ala Ile Glu Val Glu Gly Ala  
 1 5 10 15

Lys Met Gln Ser Asn Lys Thr Phe Asn Leu Glu Lys Gln Asn His Thr  
 20 25 30

Pro Arg Lys His His Gln His His His Gln Gln Gln His His Gln Gln  
 35 40 45

Gln Gln Gln Gln Pro Pro Pro Pro Pro Ile Pro Ala Asn Gly Gln Gln  
 50 55 60

Ala Ser Ser Gln Asn Glu Gly Leu Thr Ile Asp Leu Lys Asn Phe Arg  
 65 70 75 80

Lys Pro Gly Glu Lys Thr Phe Thr Gln Arg Ser Arg Leu Phe Val Gly  
 85 90 95

Asn Leu Pro Pro Asp Ile Thr Glu Glu Glu Met Arg Lys Leu Phe Glu  
 100 105 110

Lys Tyr Gly Lys Ala Gly Glu Val Phe Ile His Lys Asp Lys Gly Phe  
 115 120 125

Gly Phe Ile Arg Leu Glu Thr Arg Thr Leu Ala Glu Ile Ala Lys Val  
 130 135 140

Glu Leu Asp Asn Met Pro Leu Arg Gly Lys Gln Leu Arg Val Arg Phe  
 145 150 155 160

Ala Cys His Ser Ala Ser Leu Thr Val Arg Asn Leu Pro Gln Tyr Val  
 165 170 175

Ser Asn Glu Leu Leu Glu Glu Ala Phe Ser Val Phe Gly Gln Val Glu  
 180 185 190

Arg Ala Val Val Ile Val Asp Asp Arg Gly Arg Pro Ser Gly Lys Gly  
 195 200 205

428

Ile Val Glu Phe Ser Gly Lys Pro Ala Ala Arg Lys Ala Leu Asp Arg  
           210                          215                          220  
 Cys Ser Glu Gly Ser Phe Leu Leu Thr Thr Phe Pro Arg Pro Val Thr  
 225                          230                          235                          240  
 Val Glu Pro Met Asp Gln Leu Asp Asp Glu Glu Gly Leu Pro Glu Lys  
                           245                          250                          255  
 Leu Val Ile Lys Asn Gln Gln Phe His Lys Glu Arg Glu Gln Pro Pro  
                           260                          265                          270  
 Arg Phe Ala Gln Pro Gly Ser Phe Xaa Val  
           275                          280

<210> 479  
 <211> 289  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (206)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (215)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (218)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (285)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 479  
 Ala Val Pro Val Arg Asn Ser Arg Val Asp Pro Arg Val Arg Val Cys  
       1                          5                          10                          15

Gly Pro Leu Ser Ala Pro Arg Gly Ser Arg Arg Pro Thr Val Pro Gly  
           20                          25                          30

Thr Pro Ala Cys Leu Ala Arg Pro Ala Ala Gln Gly Phe Ser Ala Ala

429

35	40	45
Leu Pro Val Arg Trp Thr Gly Arg Arg Ala Gly Pro Ser Arg Pro Val		
50	55	60
Pro Ile Gly Thr Pro Ser Arg Ala Ala Asp Pro Ser Gln Gly Glu Met		
65	70	75
Ser Ala Asp Ala Ala Ala Gly Ala Pro Leu Pro Arg Leu Cys Cys Leu		
85	90	95
Glu Lys Gly Pro Asn Gly Tyr Gly Phe His Leu His Gly Glu Lys Gly		
100	105	110
Lys Leu Gly Gln Tyr Ile Arg Leu Val Glu Pro Gly Ser Pro Ala Glu		
115	120	125
Lys Ala Gly Leu Leu Ala Gly Asp Arg Leu Val Glu Val Asn Gly Glu		
130	135	140
Asn Val Glu Lys Glu Thr His Gln Gln Val Val Ser Arg Ile Arg Ala		
145	150	155
Ala Leu Asn Ala Val Arg Leu Leu Val Val Asp Pro Glu Thr Asp Glu		
165	170	175
Gln Leu Gln Lys Leu Gly Val Gln Val Arg Glu Glu Leu Leu Arg Ala		
180	185	190
Gln Glu Ala Pro Gly Gln Ala Glu Pro Pro Ala Ala Ala Xaa Val Gln		
195	200	205
Gly Ala Gly Asn Glu Asn Xaa Pro Arg Xaa Ala Asp Lys Ser His Pro		
210	215	220
Glu Gln Arg Glu Leu Arg Pro Arg Leu Cys Thr Met Lys Lys Gly Pro		
225	230	235
Ser Gly Tyr Gly Phe Asn Leu His Ser Asp Lys Ser Lys Pro Gly Gln		
245	250	255
Phe Ile Arg Ser Val Asp Pro Asp Ser Pro Ala Glu Ala Ser Gly Leu		
260	265	270
Arg Ala Gln Asp Arg Ile Val Glu Val Met Leu Leu Xaa Ser Leu Pro		
275	280	285
Ile		

430

<210> 480  
<211> 44  
<212> PRT  
<213> Homo sapiens

<400> 480  
Gly Ser Thr His Ala Ser Gly Arg Asn Glu Gly Pro Pro Ala Lys Thr  
1 5 10 15  
Lys Ser Trp Val Gly Pro Thr Leu His Phe His Arg Lys Ser Glu His  
20 25 30  
Leu Val Gly Leu Lys Val Leu Cys Cys Phe Arg Leu  
35 40

<210> 481  
<211> 124  
<212> PRT  
<213> Homo sapiens

<220>  
<221> SITE  
<222> (3)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (5)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (8)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (9)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (10)  
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 481  
Ser Ile Xaa His Xaa Arg Lys Xaa Xaa Xaa Thr Val Arg Ser Asp Ser  
1 5 10 15

431

Arg Val Asp Pro Arg Ser Asp Asp Phe Thr Pro Leu Glu Ile Leu Trp  
                   20                  25                  30  
 Thr Phe Ser Ile Tyr Leu Glu Ser Val Ala Ile Leu Pro Gln Leu Phe  
                   35                  40                  45  
 Met Val Ser Lys Thr Gly Glu Ala Glu Thr Ile Thr Ser His Tyr Leu  
                   50                  55                  60  
 Phe Ala Leu Gly Val Tyr Arg Thr Leu Tyr Leu Phe Asn Trp Ile Trp  
                   65                  70                  75                  80  
 Arg Tyr His Phe Glu Gly Phe Phe Asp Leu Ile Ala Ile Val Ala Gly  
                   85                  90                  95  
 Leu Val Gln Thr Val Leu Tyr Cys Asp Phe Phe Tyr Leu Tyr Ile Thr  
                   100                  105                  110  
 Lys Val Leu Lys Gly Lys Lys Leu Ser Leu Pro Ala  
                   115                  120

&lt;210&gt; 482

&lt;211&gt; 131

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (122)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (124)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (127)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (131)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 482

Cys Ser Ser Arg Gly Ala His His Ser His Cys Asp Arg Leu Pro His

432

```

      1             5             10             15
Ser Pro Trp Pro Gly Leu Arg Glu Val Glu Leu Leu Ala Ser Val His
      20             25             30
Thr Glu Gln Met Glu Glu Glu Leu Ala Leu Gly Pro Arg Gly Gln Gly
      35             40             45
Gly Ala Ser Leu Ala Gly Arg Asp Gly Arg Ser Ala Gly Ala Gly Ser
      50             55             60
Tyr Gly Ala Leu Ala Asn Ser Ala Trp Gly Gly Pro Arg Lys Val Ala
      65             70             75             80
Ser Ala Ser Ala Ala Ala Ser Thr Leu Ser Glu Pro Pro Arg Arg Thr
      85             90             95
Gln Glu Ser Arg Thr Arg Thr Arg Ala Leu Gly Leu Pro Thr Leu Pro
      100            105            110
Met Glu Lys Leu Ala Ala Ser Asn Arg Xaa Pro Xaa Gly Leu Xaa Gly
      115            120            125
Pro Gly Xaa
      130

```

&lt;210&gt; 483

&lt;211&gt; 221

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (168)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (174)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 483

```

Lys Lys Pro Pro Ile Thr His Pro Ser Thr Pro Ala Glu Glu Thr Tyr
  1             5             10             15

```

```

Asn Leu Gly Arg Gln Val Leu Pro Leu Ser Ala Val Thr Tyr Phe Gln
      20             25             30

```

```

Lys Ser Gly Pro Gly Leu Leu Pro Ala Pro Ala Thr Gln Ser Ala Ser

```

433

35	40	45
Val Ala Gly Thr Leu Gln Asn Ser Leu Cys Ser Gln Val Thr Lys Lys		
50	55	60
Lys Arg Ala Asn Met Leu Val Leu Leu Ala Gly Ile Phe Val Val His		
65	70	75 80
Ile Ala Thr Val Ile Met Leu Phe Val Ser Thr Ile Ala Asn Val Trp		
	85 90	95
Leu Val Ser Asn Thr Val Asp Ala Ser Val Gly Leu Trp Lys Asn Cys		
	100 105	110
Thr Asn Ile Ser Cys Ser Asp Ser Leu Ser Tyr Ala Ser Glu Asp Ala		
	115 120	125
Leu Lys Thr Val Gln Ala Phe Met Ile Leu Ser Ile Ile Phe Cys Val		
	130 135	140
Ile Ala Leu Leu Val Phe Val Phe Gln Leu Phe Thr Met Glu Lys Gly		
145	150	155 160
Asn Arg Phe Phe Leu Ser Gly Xaa Thr Thr Leu Val Cys Xaa Leu Cys		
	165 170	175
Ile Leu Val Gly Cys Pro Ser Thr Leu Val Ile Met Arg Ile Val Met		
	180 185	190
Glu Arg Ile Cys Thr Thr Ala Ile Pro Thr Ser Trp Ala Gly Ser Ala		
	195 200	205
Ser Ala Ser Ala Ser Ser Ser Ala Phe Ser Ile Trp Ser		
	210 215	220

&lt;210&gt; 484

&lt;211&gt; 382

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (22)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (54)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

434

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (69)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (287)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (298)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (324)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (358)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 484

Thr	Lys	Leu	Trp	Thr	Leu	Val	Ser	Asn	Pro	Asp	Thr	Asp	Ala	Leu	Ile
1				5					10					15	

Cys	Trp	Ser	Pro	Ser	Xaa	Asn	Ser	Phe	His	Val	Phe	Asp	Gln	Gly	Gln
			20					25					30		

Phe	Ala	Lys	Glu	Val	Leu	Pro	Lys	Tyr	Phe	Lys	His	Asn	Asn	Met	Ala
		35					40					45			

Ser	Phe	Val	Arg	Gln	Xaa	Asn	Met	Tyr	Gly	Phe	Arg	Lys	Val	Val	His
	50					55					60				

Ile	Glu	Gln	Gly	Xaa	Leu	Val	Lys	Pro	Glu	Arg	Asp	Asp	Thr	Glu	Phe
65					70					75				80	

Gln	His	Pro	Cys	Phe	Leu	Arg	Gly	Gln	Glu	Gln	Leu	Leu	Glu	Asn	Ile
				85					90					95	

Lys	Arg	Lys	Val	Thr	Ser	Val	Ser	Thr	Leu	Lys	Ser	Glu	Asp	Ile	Lys
			100					105					110		

Ile	Arg	Gln	Asp	Ser	Val	Thr	Lys	Leu	Leu	Thr	Asp	Val	Gln	Leu	Met
		115					120					125			



435

Lys Gly Lys Gln Glu Cys Met Asp Ser Lys Leu Leu Ala Met Lys His  
 130 135 140  
 Glu Asn Glu Ala Leu Trp Arg Glu Val Ala Ser Leu Arg Gln Lys His  
 145 150 155 160  
 Ala Gln Gln Gln Lys Val Val Asn Lys Leu Ile Gln Phe Leu Ile Ser  
 165 170 175  
 Leu Val Gln Ser Asn Arg Ile Leu Gly Val Lys Arg Lys Ile Pro Leu  
 180 185 190  
 Met Leu Asn Asp Ser Gly Ser Ala His Ser Met Pro Lys Tyr Ser Arg  
 195 200 205  
 Gln Phe Ser Leu Glu His Val His Gly Ser Gly Pro Tyr Ser Ala Pro  
 210 215 220  
 Ser Pro Ala Tyr Ser Ser Ser Ser Leu Tyr Ala Pro Asp Ala Val Ala  
 225 230 235 240  
 Ser Ser Gly Pro Ile Ile Ser Asp Ile Thr Glu Leu Ala Pro Ala Ser  
 245 250 255  
 Pro Met Ala Ser Pro Gly Gly Ser Ile Asp Glu Arg Pro Leu Ser Ser  
 260 265 270  
 Ser Pro Leu Val Arg Val Lys Glu Glu Pro Pro Ser Pro Pro Xaa Ser  
 275 280 285  
 Pro Arg Val Glu Glu Ala Ser Pro Gly Xaa Pro Ser Ser Val Asp Thr  
 290 295 300  
 Leu Leu Ser Pro Thr Ala Leu Ile Asp Ser Ile Leu Arg Glu Ser Glu  
 305 310 315 320  
 Pro Ala Pro Xaa Ser Val Thr Ala Leu Thr Asp Ala Arg Gly His Thr  
 325 330 335  
 Asp Thr Glu Gly Arg Pro Pro Ser Pro Pro Pro Thr Ser Thr Pro Glu  
 340 345 350  
 Lys Cys Leu Ser Val Xaa Ala Trp Thr Arg Met Ser Ser Val Thr Thr  
 355 360 365  
 Trp Met Leu Trp Thr Pro Thr Trp Ile Thr Cys Arg Pro Cys  
 370 375 380

&lt;210&gt; 485

436

&lt;211&gt; 416

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (399)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 485

Pro Ser Val Ala Asn Val Gly Ser His Cys Asp Leu Ser Leu Lys Ile  
 1 5 10 15

Pro Glu Ile Ser Ile Gln Asp Met Thr Ala Gln Val Thr Ser Pro Ser  
 20 25 30

Gly Lys Thr His Glu Ala Glu Ile Val Glu Gly Glu Asn His Thr Tyr  
 35 40 45

Cys Ile Arg Phe Val Pro Ala Glu Met Gly Thr His Thr Val Ser Val  
 50 55 60

Lys Tyr Lys Gly Gln His Val Pro Gly Ser Pro Phe Gln Phe Thr Val  
 65 70 75 80

Gly Pro Leu Gly Glu Gly Gly Ala His Lys Val Arg Ala Gly Gly Pro  
 85 90 95

Gly Leu Glu Arg Ala Glu Ala Gly Val Pro Ala Glu Phe Ser Ile Trp  
 100 105 110

Thr Arg Glu Ala Gly Ala Gly Gly Leu Ala Ile Ala Val Glu Gly Pro  
 115 120 125

Ser Lys Ala Glu Ile Ser Phe Glu Asp Arg Lys Asp Gly Ser Cys Gly  
 130 135 140

Val Ala Tyr Val Val Gln Glu Pro Gly Asp Tyr Glu Val Ser Val Lys  
 145 150 155 160

Phe Asn Glu Glu His Ile Pro Asp Ser Pro Phe Val Val Pro Val Ala  
 165 170 175

Ser Pro Ser Gly Asp Ala Arg Arg Leu Thr Val Ser Ser Leu Gln Glu  
 180 185 190

Ser Gly Leu Lys Val Asn Gln Pro Ala Ser Phe Ala Val Ser Leu Asn  
 195 200 205

Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His Ser Pro Ser Gly Ala  
 210 215 220

437

Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln Asp Lys Tyr Ala Val  
 225 230 235 240  
 Arg Phe Ile Pro Arg Glu Asn Gly Val Tyr Leu Ile Asp Val Lys Phe  
 245 250 255  
 Asn Gly Thr His Ile Pro Gly Ser Pro Phe Lys Ile Arg Val Gly Glu  
 260 265 270  
 Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser Ala Tyr Gly Ala Gly  
 275 280 285  
 Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu Phe Val Val Asn Thr  
 290 295 300  
 Ser Asn Ala Gly Ala Gly Ala Leu Ser Val Thr Ile Asp Gly Pro Ser  
 305 310 315 320  
 Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu Gly Tyr Arg Val Thr  
 325 330 335  
 Tyr Thr Pro Met Ala Pro Gly Ser Tyr Leu Ile Ser Ile Lys Tyr Gly  
 340 345 350  
 Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys Ala Lys Val Thr Gly  
 355 360 365  
 Pro Arg Leu Val Ser Asn His Ser Leu His Glu Thr Ser Ser Val Phe  
 370 375 380  
 Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro Gln His Gly Xaa Pro  
 385 390 395 400  
 Gly Pro Gly Pro Ala Asp Ala Ser Lys Val Val Ala Lys Gly Trp Gly  
 405 410 415

&lt;210&gt; 486

&lt;211&gt; 46

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 486

Phe Val Thr Ser Gly Lys Ile Ser Leu Tyr Val Tyr Ile Leu Thr Ile  
 1 5 10 15

438

Arg Leu Asp Thr Asn Lys Ala Thr Leu Leu Thr Ala Ser Gly Glu Leu  
 20 25 30

Ile Leu Phe Leu Ile Phe Phe Asn Lys Asp Ile Leu Arg Tyr  
 35 40 45

&lt;210&gt; 487

&lt;211&gt; 162

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 487

Leu Gly Val Ala Leu Gly Ala Val Pro Lys Leu His Leu Gly Val Leu  
 1 5 10 15

Val Ser Thr Gly Leu Arg Thr Ala Val Gly Ser Pro Arg Leu Pro Pro  
 20 25 30

Thr Ala Leu Gly Ala Ala Tyr Gly Thr Ala Lys Ser Gly Thr Gly Ile  
 35 40 45

Ala Ala Met Ser Val Met Arg Pro Glu Gln Ile Met Lys Ser Ile Ile  
 50 55 60

Pro Val Val Met Ala Gly Ile Ile Ala Ile Tyr Gly Leu Val Val Ala  
 65 70 75 80

Val Leu Ile Ala Asn Ser Leu Asn Asp Asp Ile Ser Leu Tyr Lys Ser  
 85 90 95

Phe Leu Gln Leu Gly Ala Gly Leu Ser Val Gly Leu Ser Gly Leu Ala  
 100 105 110

Ala Gly Phe Ala Ile Gly Ile Val Gly Asp Ala Gly Val Arg Gly Thr  
 115 120 125

Ala Gln Gln Pro Arg Leu Phe Val Gly Met Ile Leu Ile Leu Ile Phe  
 130 135 140

Ala Glu Val Leu Gly Leu Tyr Gly Leu Ile Val Ala Leu Ile Leu Ser  
 145 150 155 160

Thr Lys

&lt;210&gt; 488

&lt;211&gt; 114

439

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (95)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (111)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (113)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 488

Gln	Ala	Leu	Arg	Pro	Gly	Ser	Phe	Arg	Gly	Thr	Gly	Arg	Lys	Arg	Glu
1				5					10					15	

Arg	Glu	Arg	Glu	Arg	Met	Ser	Leu	Ser	Asp	Trp	His	Leu	Ala	Val	Lys
	20						25						30		

Leu	Ala	Asp	Gln	Pro	Leu	Ala	Pro	Lys	Ser	Ile	Leu	Gln	Leu	Pro	Glu
	35					40						45			

Ser	Glu	Leu	Gly	Glu	Tyr	Ser	Leu	Gly	Gly	Tyr	Ser	Ile	Ser	Phe	Leu
	50					55					60				

Lys	Gln	Leu	Ile	Ala	Gly	Lys	Leu	Gln	Glu	Ser	Val	Pro	Asp	Pro	Glu
65					70				75					80	

Leu	Ile	Asp	Leu	Ile	Tyr	Cys	Gly	Arg	Lys	Leu	Lys	Asp	Asp	Xaa	Thr
			85						90					95	

Leu	Thr	Ser	Thr	Val	Phe	Asn	Leu	Ala	Pro	His	Pro	Cys	Ser	Xaa	Glu
			100					105						110	

Xaa Leu

&lt;210&gt; 489

&lt;211&gt; 149

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

440

&lt;221&gt; SITE

&lt;222&gt; (121)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (142)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 489

Ser	Thr	His	Ala	Ser	Glu	Asp	Val	Leu	Ala	Ala	Pro	Ser	Gly	Cys	Arg
1				5				10						15	

Ala	Ser	Arg	Pro	Pro	Thr	Ser	Gly	Arg	Glu	Gln	Phe	Trp	Ala	Arg	Gly
			20					25					30		

Leu	Ala	Ala	Ala	Asp	Met	Thr	Lys	Gly	Leu	Val	Leu	Gly	Ile	Tyr	Ser
			35				40					45			

Lys	Asp	Lys	Glu	Asp	Asp	Val	Pro	Gln	Phe	Thr	Ser	Ala	Gly	Glu	Asn
	50					55					60				

Phe	Asp	Lys	Leu	Val	Ser	Gly	Lys	Leu	Arg	Glu	Ile	Leu	Asn	Ile	Ser
65					70				75						80

Gly	Pro	Pro	Leu	Lys	Ala	Gly	Lys	Thr	Arg	Thr	Phe	Tyr	Gly	Leu	His
				85					90					95	

Glu	Asp	Phe	Pro	Ser	Val	Val	Val	Val	Gly	Leu	Gly	Arg	Lys	Ala	Ala
			100						105				110		

Gly	Val	Asp	Asp	Gln	Glu	Asn	Trp	Xaa	Glu	Gly	Lys	Glu	Asn	Ile	Arg
		115					120					125			

Val	Ala	Met	Gln	Arg	Gly	Ala	Gly	Arg	Phe	Gln	Asp	Leu	Xaa	Ile	Ser
		130				135						140			

Ser	Val	Glu	Gly	Gly
145				

&lt;210&gt; 490

&lt;211&gt; 527

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (311)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

441

&lt;400&gt; 490

Arg Arg Arg Ser Arg Gly Leu Ile Pro Gly Arg Ala Pro Gly Arg Arg  
 1 5 10 15

Arg Pro Arg Ala His Glu Val Ala Arg Ala Pro Pro Pro Ile Ala Met  
 20 25 30

Asp Arg Met Lys Lys Ile Lys Arg Gln Leu Ser Met Thr Leu Arg Gly  
 35 40 45

Gly Arg Gly Ile Asp Lys Thr Asn Gly Ala Pro Glu Gln Ile Gly Leu  
 50 55 60

Asp Glu Ser Gly Gly Gly Gly Gly Ser Asp Pro Gly Glu Ala Pro Thr  
 65 70 75 80

Arg Ala Ala Pro Gly Glu Leu Arg Ser Ala Arg Gly Pro Leu Ser Ser  
 85 90 95

Ala Pro Glu Ile Val His Glu Asp Leu Lys Met Gly Ser Asp Gly Glu  
 100 105 110

Ser Asp Gln Ala Ser Ala Thr Ser Ser Asp Glu Val Gln Ser Pro Val  
 115 120 125

Arg Val Arg Met Arg Asn His Pro Pro Arg Lys Ile Ser Thr Glu Asp  
 130 135 140

Ile Asn Lys Arg Leu Ser Leu Pro Ala Asp Ile Arg Leu Pro Glu Gly  
 145 150 155 160

Tyr Leu Glu Lys Leu Thr Leu Asn Ser Pro Ile Phe Asp Lys Pro Leu  
 165 170 175

Ser Arg Arg Leu Arg Arg Val Ser Leu Ser Glu Ile Gly Phe Gly Lys  
 180 185 190

Leu Glu Thr Tyr Ile Lys Leu Asp Lys Leu Gly Glu Gly Thr Tyr Ala  
 195 200 205

Thr Val Tyr Lys Gly Lys Ser Lys Leu Thr Asp Asn Leu Val Ala Leu  
 210 215 220

Lys Glu Ile Arg Leu Glu His Glu Glu Gly Ala Pro Cys Thr Ala Ile  
 225 230 235 240

Arg Glu Val Ser Leu Lys Asp Leu Lys His Ala Asn Ile Val Thr  
 245 250 255

Leu His Asp Ile Ile His Thr Glu Lys Ser Leu Thr Leu Val Phe Glu

442

260	265	270
Tyr Leu Asp Lys Asp Leu Lys Gln Tyr Leu Asp Asp Cys Gly Asn Ile		
275	280	285
Ile Asn Met His Asn Val Lys Leu Phe Leu Phe Gln Leu Leu Arg Gly		
290	295	300
Leu Ala Tyr Cys His Arg Xaa Lys Val Leu His Arg Asp Leu Lys Pro		
305	310	315 320
Gln Asn Leu Leu Ile Asn Glu Arg Gly Glu Leu Lys Leu Ala Asp Phe		
	325	330 335
Gly Leu Ala Arg Ala Lys Ser Ile Pro Thr Lys Thr Tyr Ser Asn Glu		
	340	345 350
Val Val Thr Leu Trp Tyr Arg Pro Pro Asp Ile Leu Leu Gly Ser Thr		
	355	360 365
Asp Tyr Ser Thr Gln Ile Asp Met Trp Gly Val Gly Cys Ile Phe Tyr		
	370	375 380
Glu Met Ala Thr Gly Arg Pro Leu Phe Pro Gly Ser Thr Val Glu Glu		
	385	390 395 400
Gln Leu His Phe Ile Phe Arg Ile Leu Gly Thr Pro Thr Glu Glu Thr		
	405	410 415
Trp Pro Gly Ile Leu Ser Asn Glu Glu Phe Lys Thr Tyr Asn Tyr Pro		
	420	425 430
Lys Tyr Arg Ala Glu Ala Leu Leu Ser His Ala Pro Arg Leu Asp Ser		
	435	440 445
Asp Gly Ala Asp Leu Leu Thr Lys Leu Leu Gln Phe Glu Gly Arg Asn		
	450	455 460
Arg Ile Ser Ala Glu Asp Ala Met Lys His Pro Phe Phe Leu Ser Leu		
	465	470 475 480
Gly Glu Arg Ile His Lys Leu Pro Asp Thr Thr Ser Ile Phe Ala Leu		
	485	490 495
Lys Glu Ile Gln Leu Gln Lys Glu Ala Ser Leu Arg Ser Ser Ser Met		
	500	505 510
Pro Asp Ser Gly Arg Pro Ala Phe Arg Val Val Asp Thr Glu Phe		
	515	520 525



443

<210> 491  
<211> 125  
<212> PRT  
<213> Homo sapiens

<220>  
<221> SITE  
<222> (125)  
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 491  
Cys Thr Arg Ala His Pro Lys Asn Leu Val Glu Lys Gly Ile Leu Thr  
1 5 10 15  
Thr Glu Lys Gln Asn Phe Leu Leu Phe Asp Met Thr Thr His Pro Val  
20 25 30  
Thr Asn Thr Thr Glu Lys Gln Arg Leu Val Lys Lys Leu Gln Asp Ser  
35 40 45  
Val Leu Glu Arg Trp Val Asn Asp Pro Gln Arg Met Asp Lys Arg Thr  
50 55 60  
Leu Ala Leu Leu Val Leu Ala His Ser Ser Asp Val Leu Glu Asn Val  
65 70 75 80  
Phe Ser Ser Leu Thr Asp Asp Lys Tyr Asp Val Ala Met Asn Arg Ala  
85 90 95  
Lys Asp Leu Val Glu Leu Asp Pro Glu Val Glu Gly Thr Lys Pro Ser  
100 105 110  
Ala Thr Glu Met Ile Trp Ala Val Leu Ala Ala Phe Xaa  
115 120 125

<210> 492  
<211> 53  
<212> PRT  
<213> Homo sapiens

<220>  
<221> SITE  
<222> (3)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (49)

444

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (51)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 492

Val	Ser	Xaa	Ser	Ile	Leu	Ala	Leu	Leu	Phe	Asn	Thr	Asp	Ala	Leu	Phe
1				5					10					15	

Ser	Arg	Val	Tyr	Glu	Ser	Leu	Ser	Asp	Asn	His	Gly	Leu	Gln	Glu	Gln
			20					25					30		

Thr	Val	Glu	Lys	Leu	Phe	Phe	Gln	Trp	Lys	Ser	Trp	Val	Gln	Glu	Met
			35				40					45			

Xaa	Gly	Xaa	Leu	Lys
				50

<210> 493

<211> 82

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (60)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (67)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (68)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (78)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (79)

<223> Xaa equals any of the naturally occurring L-amino acids

.445

&lt;400&gt; 493

Pro Gly Phe Phe Phe Gln Met Leu Val His Thr Tyr Ser Ser Met Asp  
 1 5 10 15

Arg His Asp Gly Val Pro Ser His Ser Ser Arg Leu Ser Gln Leu Gly  
 20 25 30

Ser Val Ser Gln Gly Pro Tyr Ser Ser Ala Pro Pro Leu Ser His Thr  
 35 40 45

Pro Ser Ser Asp Phe Gln Pro Pro Tyr Phe Pro Xaa Pro Tyr Gln Pro  
 50 55 60

Leu Pro Xaa Xaa Gln Ser Gln Asp Pro Tyr Ser His Val Xaa Xaa Pro  
 65 70 75 80

Tyr Pro

&lt;210&gt; 494

&lt;211&gt; 290

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 494

Tyr Lys Asp Trp Leu Thr Lys Met Ser Gly Lys His Asp Val Gly Ala  
 1 5 10 15

Tyr Met Leu Met Tyr Lys Gly Ala Asn Arg Thr Glu Thr Val Thr Ser  
 20 25 30

Phe Arg Lys Arg Glu Ser Lys Val Pro Ala Asp Leu Leu Lys Arg Ala  
 35 40 45

Phe Val Arg Met Ser Thr Ser Pro Glu Ala Phe Leu Ala Leu Arg Ser  
 50 55 60

His Phe Ala Ser Ser His Ala Leu Ile Cys Ile Ser His Trp Ile Leu  
 65 70 75 80

Gly Ile Gly Asp Arg His Leu Asn Asn Phe Met Val Ala Met Glu Thr  
 85 90 95

Gly Gly Val Ile Gly Ile Asp Phe Gly His Ala Phe Gly Ser Ala Thr  
 100 105 110

Gln Phe Leu Pro Val Pro Glu Leu Met Pro Phe Arg Leu Thr Arg Gln  
 115 120 125

446

Phe Ile Asn Leu Met Leu Pro Met Lys Glu Thr Gly Leu Met Tyr Ser  
 130 135 140  
 Ile Met Val His Ala Leu Arg Ala Phe Arg Ser Asp Pro Gly Leu Leu  
 145 150 155 160  
 Thr Asn Thr Met Asp Val Phe Val Lys Glu Pro Ser Phe Asp Trp Lys  
 165 170 175  
 Asn Phe Glu Gln Lys Met Leu Lys Lys Gly Gly Ser Trp Ile Gln Glu  
 180 185 190  
 Ile Asn Val Ala Glu Lys Asn Trp Tyr Pro Arg Gln Lys Ile Cys Tyr  
 195 200 205  
 Ala Lys Arg Lys Leu Ala Gly Ala Asn Pro Ala Val Ile Thr Cys Asp  
 210 215 220  
 Glu Leu Leu Leu Gly His Glu Lys Ala Pro Ala Phe Arg Asp Tyr Val  
 225 230 235 240  
 Ala Val Ala Arg Gly Ser Lys Asp His Asn Ile Arg Ala Gln Glu Pro  
 245 250 255  
 Glu Ser Gly Leu Ser Glu Glu Thr Gln Val Lys Cys Leu Met Asp Gln  
 260 265 270  
 Ala Thr Asp Pro Asn Ile Leu Gly Arg Thr Trp Glu Gly Trp Glu Pro  
 275 280 285  
 Trp Met  
 290

&lt;210&gt; 495

&lt;211&gt; 156

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (148)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 495

Cys Gln Ser His Pro Leu Pro Gly Gly Pro Ala Cys Pro Cys Leu Ala  
 1 5 10 15

Cys His Ile Thr Leu Leu Phe Gly Arg Pro Trp Leu Ile Lys Glu Val

447

20                      25                      30  
 Leu Val Val Ser Gln Ala Lys Trp Asn Leu Glu Thr Val Lys Lys Val  
           35                      40                      45  
 Gln Ile Thr Leu Asn Cys Ile Gln Glu Val His Phe Phe Pro Ile Val  
           50                      55                      60  
 Arg Gly Ser Trp Ser Leu Arg Asp Ala Arg Leu Glu Ser Asp Tyr Ile  
           65                      70                      75                      80  
 Ile Ile Gln Asn Gly Asn Ser Gln Gly Asn Ala Phe Phe His Phe Ile  
                           85                      90                      95  
 Arg Phe Phe Tyr Pro His Cys Thr Pro Ser Pro Ser Pro Leu Pro Ile  
                           100                      105                      110  
 Trp Met Ala Ser Gln Lys Leu Gly Pro Ser Pro Pro Cys Leu Gly Gly  
           115                      120                      125  
 Gly Gln Ser Pro Leu Thr Ala Glu Ala Ala Leu Leu Ser Ser Ala Val  
           130                      135                      140  
 Leu Pro Leu Xaa Lys Cys Leu Gln Arg Val Met Ser  
           145                      150                      155

&lt;210&gt; 496

&lt;211&gt; 251

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (42)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 496

Glu Glu Leu Leu Arg Ala Gln Glu Ala Pro Gly Gln Ala Glu Pro Pro  
           1                      5                      10                      15  
 Ala Ala Ala Glu Val Gln Gly Ala Gly Asn Glu Asn Glu Pro Arg Glu  
                           20                      25                      30  
 Ala Asp Lys Ser His Pro Glu Gln Arg Xaa Leu Arg Pro Arg Leu Cys  
           35                      40                      45  
 Thr Met Lys Lys Gly Pro Ser Gly Tyr Gly Phe Asn Leu His Ser Asp  
           50                      55                      60

448

Lys Ser Lys Pro Gly Gln Phe Ile Arg Ser Val Asp Pro Asp Ser Pro  
 65 70 75 80  
 Ala Glu Ala Ser Gly Leu Arg Ala Gln Asp Arg Ile Val Glu Val Asn  
 85 90 95  
 Gly Val Cys Met Glu Gly Lys Gln His Gly Asp Val Val Ser Ala Ile  
 100 105 110  
 Arg Ala Gly Gly Asp Glu Thr Lys Leu Leu Val Val Asp Arg Glu Thr  
 115 120 125  
 Asp Glu Phe Phe Lys Lys Cys Arg Val Ile Pro Ser Gln Glu His Leu  
 130 135 140  
 Asn Gly Pro Leu Pro Val Pro Phe Thr Asn Gly Glu Ile Gln Lys Glu  
 145 150 155 160  
 Asn Ser Arg Glu Ala Leu Ala Glu Ala Ala Leu Glu Ser Pro Arg Pro  
 165 170 175  
 Ala Leu Val Arg Ser Ala Ser Ser Asp Thr Ser Glu Glu Leu Asn Ser  
 180 185 190  
 Gln Asp Ser Pro Pro Lys Gln Asp Ser Thr Ala Pro Ser Ser Thr Ser  
 195 200 205  
 Ser Ser Asp Pro Ile Leu Asp Phe Asn Ile Ser Leu Ala Met Ala Lys  
 210 215 220  
 Glu Arg Ala His Gln Lys Arg Ser Ser Lys Arg Ala Pro Gln Met Asp  
 225 230 235 240  
 Trp Ser Lys Lys Asn Glu Leu Phe Ser Asn Leu  
 245 250

&lt;210&gt; 497

&lt;211&gt; 48

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 497

Asn Gly Ala Glu Ala Val Ser Thr Glu Ala Lys Met Thr Ala Phe Pro  
 1 5 10 15  
 Asp Trp Pro Trp Leu Phe His Thr Leu Cys Asp Pro Cys Pro Met Thr  
 20 25 30  
 Leu Trp Leu Thr Leu Pro Glu Ala Met Thr Thr Ala Ala Phe Cys His

449

35

40

45

&lt;210&gt; 498

&lt;211&gt; 373

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (337)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (372)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 498

Gly Thr Arg Gly Ser Arg Ala Ser Gly Val Cys Ala Arg Gly Cys Leu  
 1 5 10 15

Asp Ser Ala Gly Pro Trp Thr Met Ser Arg Ala Leu Arg Pro Pro Leu  
 20 25 30

Pro Pro Leu Cys Phe Phe Leu Leu Leu Leu Ala Ala Ala Gly Ala Arg  
 35 40 45

Ala Gly Gly Tyr Glu Thr Cys Pro Thr Val Gln Pro Asn Met Leu Asn  
 50 55 60

Val His Leu Leu Pro His Thr His Asp Asp Val Gly Trp Leu Lys Thr  
 65 70 75 80

Val Asp Gln Tyr Phe Tyr Gly Ile Lys Asn Asp Ile Gln His Ala Gly  
 85 90 95

Val Gln Tyr Ile Leu Asp Ser Val Ile Ser Ala Leu Leu Ala Asp Pro  
 100 105 110

Thr Arg Arg Phe Ile Tyr Val Glu Ile Ala Phe Phe Ser Arg Trp Trp  
 115 120 125

His Gln Gln Thr Asn Ala Thr Gln Glu Val Val Arg Asp Leu Val Arg  
 130 135 140

Gln Gly Arg Leu Glu Phe Ala Asn Gly Gly Trp Val Met Asn Asp Glu

450

145		150		155		160
Ala Ala Thr His Tyr Gly Ala Ile Val Asp Gln Met Thr Leu Gly Leu						
	165		170		175	
Arg Phe Leu Glu Asp Thr Phe Gly Asn Asp Gly Arg Pro Arg Val Ala						
	180		185		190	
Trp His Ile Asp Pro Phe Gly His Ser Arg Glu Gln Ala Ser Leu Phe						
	195		200		205	
Ala Gln Met Gly Phe Asp Gly Phe Phe Phe Gly Arg Leu Asp Tyr Gln						
	210		215		220	
Asp Lys Trp Val Arg Met Gln Lys Leu Glu Met Glu Gln Val Trp Arg						
	225		230		235	240
Ala Ser Thr Ser Leu Lys Pro Pro Thr Ala Asp Leu Phe Thr Gly Val						
	245		250		255	
Leu Pro Asn Gly Tyr Asn Pro Pro Arg Asn Leu Cys Trp Asp Val Leu						
	260		265		270	
Cys Val Asp Gln Pro Leu Val Glu Asp Pro Arg Ser Pro Glu Tyr Asn						
	275		280		285	
Ala Lys Glu Leu Val Asp Tyr Phe Leu Asn Val Ala Thr Ala Gln Gly						
	290		295		300	
Arg Tyr Tyr Arg Thr Asn His Thr Val Met Thr Met Gly Ser Asp Phe						
	305		310		315	320
Gln Tyr Glu Asn Ala Asn Met Trp Phe Lys Asn Leu Asp Lys Leu Ile						
	325		330		335	
Xaa Leu Val Asn Ala Gln Gly Lys Arg Lys Gln Cys Pro Cys Ser Leu						
	340		345		350	
Leu His Pro Arg Leu Leu Pro Leu Gly Ala Glu Gln Gly Gln Pro His						
	355		360		365	
Leu Val Ser Xaa Thr						
	370					

&lt;210&gt; 499

&lt;211&gt; 238

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



451

&lt;400&gt; 499

Ala Leu Pro Gly Pro Asp Trp His Gly Ala Gly Ala Ala Asp Arg Gly  
 1 5 10 15  
 Pro Ala Ala Pro Pro Arg Pro Gly Pro Cys Ala Tyr Ala Ala His Gly  
 20 25 30  
 Arg Gly Ala Leu Ala Glu Ala Ala Arg Arg Cys Leu His Asp Ile Ala  
 35 40 45  
 Leu Ala His Arg Ala Ala Thr Ala Ala Arg Pro Pro Ala Pro Pro Pro  
 50 55 60  
 Ala Pro Gln Pro Pro Ser Pro Thr Pro Ser Pro Pro Arg Pro Thr Leu  
 65 70 75 80  
 Ala Arg Glu Asp Asn Glu Glu Asp Glu Asp Glu Pro Thr Glu Thr Glu  
 85 90 95  
 Thr Ser Gly Glu Gln Leu Gly Ile Ser Asp Asn Gly Gly Leu Phe Val  
 100 105 110  
 Met Asp Glu Asp Ala Thr Leu Gln Asp Leu Pro Pro Phe Cys Glu Ser  
 115 120 125  
 Asp Pro Glu Ser Thr Asp Asp Gly Ser Leu Ser Glu Glu Thr Pro Ala  
 130 135 140  
 Gly Pro Pro Thr Cys Ser Val Pro Pro Ala Ser Ala Leu Pro Thr Gln  
 145 150 155 160  
 Gln Tyr Ala Lys Ser Leu Pro Val Ser Val Pro Val Trp Gly Phe Lys  
 165 170 175  
 Glu Lys Arg Thr Glu Ala Arg Ser Ser Asp Glu Glu Asn Gly Pro Pro  
 180 185 190  
 Ser Ser Pro Asp Leu Asp Arg Ile Ala Ala Ser Met Arg Ala Leu Val  
 195 200 205  
 Leu Arg Glu Ala Glu Asp Thr Gln Val Phe Gly Asp Leu Pro Arg Pro  
 210 215 220  
 Arg Leu Asn Thr Ser Asp Phe Gln Lys Leu Lys Arg Lys Tyr  
 225 230 235

&lt;210&gt; 500

&lt;211&gt; 198

&lt;212&gt; PRT

452

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (94)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (156)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 500

Asn	Ser	Ala	Glu	Leu	Ser	Pro	Gly	Leu	Cys	Ser	Pro	Thr	Pro	Thr	Glu
1				5					10					15	

Ala	Arg	Ala	Gly	Asp	Ala	Gly	Pro	Ala	Ala	Arg	Ser	Arg	Lys	Gln	Asn
			20					25					30		

Pro	Gln	Ser	Pro	Pro	Cys	Cys	Cys	Val	Asp	Asp	Thr	Trp	Ala	Gln	Ala
	35						40					45			

Glu	Val	Gly	Pro	Val	Thr	Ser	Cys	Thr	Gly	Phe	Val	Glu	Gly	Ser	Ser
	50					55					60				

Arg	Thr	Gly	Gly	Met	Gly	Ser	Ala	Cys	Ile	Lys	Val	Thr	Lys	Tyr	Phe
65					70					75					80

Leu	Phe	Leu	Phe	Asn	Leu	Ile	Phe	Phe	Ile	Leu	Gly	Ala	Xaa	Ile	Leu
				85					90					95	

Gly	Phe	Gly	Val	Trp	Ile	Leu	Ala	Asp	Lys	Ser	Ser	Phe	Ile	Ser	Val
			100					105					110		

Leu	Gln	Thr	Ser	Ser	Ser	Ser	Leu	Arg	Met	Gly	Ala	Tyr	Val	Phe	Ile
		115					120					125			

Gly	Val	Gly	Ala	Val	Thr	Met	Leu	Met	Gly	Phe	Leu	Gly	Cys	Ile	Gly
	130					135					140				

Ala	Val	Asn	Glu	Val	Arg	Cys	Leu	Leu	Gly	Leu	Xaa	Phe	Ala	Phe	Leu
145					150					155					160

Leu	Leu	Ile	Leu	Ile	Ala	Gln	Val	Thr	Ala	Gly	Ala	Leu	Phe	Tyr	Phe
			165						170					175	

Asn	Met	Gly	Lys	Val	Ser	Pro	Ser	Leu	Pro	Pro	Ser	Ser	Leu	Gly	Trp
			180					185					190		

Thr	Asn	His	Gly	Gly	Asp
			195		

453

&lt;210&gt; 501

&lt;211&gt; 169

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (165)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 501

Ser Ser Ala Ser Thr Asn Met Ser Arg Gly Ser Ser Ala Gly Phe Asp  
 1 5 10 15

Arg His Ile Thr Ile Phe Ser Pro Glu Gly Arg Leu Tyr Gln Val Glu  
 20 25 30

Tyr Ala Phe Lys Ala Ile Asn Gln Gly Gly Leu Thr Ser Val Ala Val  
 35 40 45

Arg Gly Lys Asp Cys Ala Val Ile Val Thr Gln Lys Lys Val Pro Asp  
 50 55 60

Lys Leu Leu Asp Ser Ser Thr Val Thr His Leu Phe Lys Ile Thr Glu  
 65 70 75 80

Asn Ile Gly Cys Val Met Thr Gly Met Thr Ala Asp Ser Arg Ser Gln  
 85 90 95

Val Gln Arg Ala Arg Tyr Glu Ala Ala Asn Trp Lys Tyr Lys Tyr Gly  
 100 105 110

Tyr Glu Ile Pro Val Asp Met Leu Cys Lys Arg Ile Ala Asp Ile Ser  
 115 120 125

Gln Val Tyr Thr Gln Asn Ala Glu Met Arg Pro Leu Gly Cys Cys Met  
 130 135 140

Ile Leu Ile Gly Ile Asp Glu Glu Gln Gly Pro Gln Val Tyr Lys Cys  
 145 150 155 160

Asp Pro Ala Gly Xaa Tyr Cys Gly Val  
 165

&lt;210&gt; 502

&lt;211&gt; 507

454

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (10)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (361)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (461)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 502

Val	Arg	Gln	Leu	Cys	Arg	Pro	Ala	Glu	Xaa	Asp	Ser	Val	Met	Ala	Glu
1				5					10					15	

Gln	Val	Ala	Leu	Ser	Arg	Thr	Gln	Val	Cys	Gly	Ile	Leu	Arg	Glu	Glu
			20					25					30		

Leu	Phe	Gln	Gly	Asp	Ala	Phe	His	Gln	Ser	Asp	Thr	His	Ile	Phe	Ile
		35					40					45			

Ile	Met	Gly	Ala	Ser	Gly	Asp	Leu	Ala	Lys	Lys	Lys	Ile	Tyr	Pro	Thr
	50					55					60				

Ile	Trp	Trp	Leu	Phe	Arg	Asp	Gly	Leu	Leu	Pro	Glu	Asn	Thr	Phe	Ile
65					70					75					80

Val	Gly	Tyr	Ala	Arg	Ser	Arg	Leu	Thr	Val	Ala	Asp	Ile	Arg	Lys	Gln
				85					90					95	

Ser	Glu	Pro	Phe	Phe	Lys	Ala	Thr	Pro	Glu	Glu	Lys	Leu	Lys	Leu	Glu
			100					105					110		

Asp	Phe	Phe	Ala	Arg	Asn	Ser	Tyr	Val	Ala	Gly	Gln	Tyr	Asp	Asp	Ala
		115					120					125			

Ala	Ser	Tyr	Gln	Arg	Leu	Asn	Ser	His	Met	Asn	Ala	Leu	His	Leu	Gly
	130					135					140				

Ser	Gln	Ala	Asn	Arg	Leu	Phe	Tyr	Leu	Ala	Leu	Pro	Pro	Thr	Val	Tyr
145					150					155					160

Glu	Ala	Val	Thr	Lys	Asn	Ile	His	Glu	Ser	Cys	Met	Ser	Gln	Ile	Gly
				165					170					175	

455

Trp Asn Arg Ile Ile Val Glu Lys Pro Phe Gly Arg Asp Leu Gln Ser  
 180 185 190  
 Ser Asp Arg Leu Ser Asn His Ile Ser Ser Leu Phe Arg Glu Asp Gln  
 195 200 205  
 Ile Tyr Arg Ile Asp His Tyr Leu Gly Lys Glu Met Val Gln Asn Leu  
 210 215 220  
 Met Val Leu Arg Phe Ala Asn Arg Ile Phe Gly Pro Ile Trp Asn Arg  
 225 230 235 240  
 Asp Asn Ile Ala Cys Val Ile Leu Thr Phe Lys Glu Pro Phe Gly Thr  
 245 250 255  
 Glu Gly Arg Gly Gly Tyr Phe Asp Glu Phe Gly Ile Ile Arg Asp Val  
 260 265 270  
 Met Gln Asn His Leu Leu Gln Met Leu Cys Leu Val Ala Met Glu Lys  
 275 280 285  
 Pro Ala Ser Thr Asn Ser Asp Asp Val Arg Asp Glu Lys Val Lys Val  
 290 295 300  
 Leu Lys Cys Ile Ser Glu Val Gln Ala Asn Asn Val Val Leu Gly Gln  
 305 310 315 320  
 Tyr Val Gly Asn Pro Asp Gly Glu Gly Glu Ala Thr Lys Gly Tyr Leu  
 325 330 335  
 Asp Asp Pro Thr Val Pro Arg Gly Ser Thr Thr Ala Thr Phe Ala Ala  
 340 345 350  
 Val Val Leu Tyr Val Glu Asn Glu Xaa Trp Asp Gly Val Pro Phe Ile  
 355 360 365  
 Leu Arg Cys Gly Lys Ala Leu Asn Glu Arg Lys Ala Glu Val Arg Leu  
 370 375 380  
 Gln Phe His Asp Val Ala Gly Asp Ile Phe His Gln Gln Cys Lys Arg  
 385 390 395 400  
 Asn Glu Leu Val Ile Arg Val Gln Pro Asn Glu Ala Val Tyr Thr Lys  
 405 410 415  
 Met Met Thr Lys Lys Pro Gly Met Phe Phe Asn Pro Glu Glu Ser Glu  
 420 425 430  
 Leu Asp Leu Thr Tyr Gly Asn Arg Tyr Lys Asn Val Lys Leu Pro Asp  
 435 440 445

456

Ala Tyr Glu Arg Leu Ile Leu Asp Val Phe Cys Gly Xaa Gln Met His  
 450 455 460

Phe Val Arg Arg Thr Ser Ser Val Arg Pro Gly Val Phe Ser Pro His  
 465 470 475 480

Cys Cys Thr Arg Leu Ser Trp Arg Ser Pro Ser Pro Ser Pro Ile Phe  
 485 490 495

Met Ala Ala Glu Ala Pro Arg Arg Gln Thr Ser  
 500 505

<210> 503

<211> 260

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (69)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 503

Gly Pro Glu Val Leu Pro Glu Pro Arg Val Pro Arg Glu Ala Leu Ala  
 1 5 10 15

Phe Ile Ile Arg Ser Phe Gly Gly Glu Val Ser Trp Asp Lys Ser Leu  
 20 25 30

Cys Ile Gly Ala Thr Tyr Asp Val Thr Asp Ser Arg Ile Thr His Gln  
 35 40 45

Ile Val Asp Arg Pro Gly Gln Gln Thr Ser Val Ile Gly Arg Cys Tyr  
 50 55 60

Val Gln Pro Gln Xaa Val Phe Asp Ser Val Asn Ala Arg Leu Leu Leu  
 65 70 75 80

Pro Val Ala Glu Tyr Phe Ser Gly Val Gln Leu Pro Pro His Leu Ser  
 85 90 95

Pro Phe Val Thr Glu Lys Glu Gly Asp Tyr Val Pro Pro Glu Lys Leu  
 100 105 110

Lys Leu Leu Ala Leu Gln Arg Gly Glu Asp Pro Gly Asn Leu Asn Glu  
 115 120 125

Ser Glu Glu Glu Glu Glu Asp Asp Asn Asn Glu Gly Asp Gly Asp

457

130                      135                      140  
 Glu Glu Gly Glu Asn Glu Glu Glu Glu Glu Asp Ala Glu Ala Gly Ser  
 145                      150                      155                      160  
 Glu Lys Glu Glu Glu Ala Arg Leu Ala Ala Leu Glu Glu Gln Arg Met  
                     165                      170                      175  
 Glu Gly Lys Lys Pro Arg Val Met Ala Gly Thr Leu Lys Leu Glu Asp  
                     180                      185                      190  
 Lys Gln Arg Leu Ala Gln Glu Glu Glu Ser Glu Ala Lys Arg Leu Ala  
                     195                      200                      205  
 Ile Met Met Met Lys Lys Arg Glu Lys Tyr Leu Tyr Gln Lys Ile Met  
                     210                      215                      220  
 Phe Gly Lys Arg Arg Lys Ile Arg Glu Ala Asn Lys Leu Ala Glu Lys  
 225                      230                      235                      240  
 Arg Lys Ala His Asp Glu Ala Val Arg Ser Glu Lys Lys Ala Lys Lys  
                     245                      250                      255  
 Ala Arg Pro Glu  
                     260

&lt;210&gt; 504

&lt;211&gt; 424

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (292)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (342)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 504

Leu Leu Gln Arg Cys Tyr Ala Phe Pro Gly His Arg Leu Ala His Ser  
 1                      5                      10                      15

Gly Ser Asp Leu Ser Leu Leu Val Pro Glu Ile Glu Asp Met Tyr Ser  
                     20                      25                      30

Ser Pro Tyr Leu Arg Pro Ser Glu Ser Pro Ile Thr Val Glu Val Asn

458

35	40	45
Cys Thr Asn Pro Gly Thr Arg Tyr Cys Trp Met Ser Thr Gly Leu Tyr		
50	55	60
Ile Pro Gly Arg Gln Ile Ile Glu Val Ser Leu Pro Glu Ala Ala Ala		
65	70	75
Ser Ala Asp Leu Lys Ile Gln Ile Gly Cys His Thr Asp Asp Leu Thr		
85	90	95
Arg Ala Ser Lys Leu Phe Arg Gly Pro Leu Val Ile Asn Arg Cys Cys		
100	105	110
Leu Asp Lys Pro Thr Lys Ser Ile Thr Cys Leu Trp Gly Gly Leu Leu		
115	120	125
Tyr Ile Ile Val Pro Gln Asn Ser Lys Leu Gly Ser Val Pro Val Thr		
130	135	140
Val Lys Gly Ala Val His Ala Pro Tyr Tyr Lys Leu Gly Glu Thr Thr		
145	150	155
Leu Glu Glu Trp Lys Arg Arg Ile Gln Glu Asn Pro Gly Pro Trp Gly		
165	170	175
Glu Leu Ala Thr Asp Asn Ile Ile Leu Thr Val Pro Thr Ala Asn Leu		
180	185	190
Arg Thr Leu Glu Asn Pro Glu Pro Leu Leu Arg Leu Trp Asp Glu Val		
195	200	205
Met Gln Ala Val Ala Arg Leu Gly Ala Glu Pro Phe Pro Leu Arg Leu		
210	215	220
Pro Gln Arg Ile Val Ala Asp Val Gln Ile Ser Val Gly Trp Met His		
225	230	235
Ala Gly Tyr Pro Ile Met Cys His Leu Glu Ser Val Gln Glu Leu Ile		
245	250	255
Asn Glu Lys Leu Ile Arg Thr Lys Gly Leu Trp Gly Pro Val His Glu		
260	265	270
Leu Gly Arg Asn Gln Gln Arg Gln Glu Trp Glu Phe Pro Pro His Thr		
275	280	285
Thr Glu Ala Xaa Cys Asn Leu Trp Cys Val Tyr Val His Glu Thr Val		
290	295	300
Leu Gly Ile Pro Arg Ser Arg Ala Asn Ile Ala Leu Trp Pro Pro Val		



459

[illegible]

<210> 505

<211> 70

<212> PRT.

<213> Homo sapiens

**<220>**

<221> SITE

<222> (49)

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

<221> SITE

<222> (54)

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

**<221> SITE**

<222> (66)

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

<221> SITE

**<222> (70)**

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 505

460

Leu His Gln Ser Leu Leu His Leu Glu Lys Thr Asn Glu Arg Lys Ser  
 1 5 10 15  
 Ile Phe Leu Ile His Tyr Pro Asn Asn Asn Arg Thr Pro Tyr Arg Asn  
 20 25 30  
 Tyr Tyr His Tyr Val Ser Lys His Tyr Ile Pro Ile Thr Tyr Pro Thr  
 35 40 45  
 Xaa Ser Ile Ile Asp Xaa Ile Ser Ile Pro Thr Met Ile Ser Ala Leu  
 50 55 60  
 Asn Xaa Gln Asn Lys Xaa  
 65 70

&lt;210&gt; 506

&lt;211&gt; 434

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (69)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (135)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (363)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 506

Ser Thr His Ala Ser Ala His Ala Ser Val Ser Thr Ala Ala Ala Ala  
 1 5 10 15  
 Ala Leu Ala Ala Ala Val Lys Ala Lys His Leu Ala Ala Val Glu  
 20 25 30  
 Glu Arg Lys Ile Lys Ser Leu Val Ala Leu Leu Val Glu Thr Gln Met  
 35 40 45  
 Lys Lys Leu Glu Ile Lys Leu Arg His Phe Glu Glu Leu Glu Thr Ile  
 50 55 60  
 Met Asp Arg Glu Xaa Glu Ala Leu Glu Tyr Gln Arg Gln Gln Leu Leu

461

65	70	75	80
Ala Asp Arg Gln Ala Phe His Met Glu Gln Leu Lys Tyr Ala Glu Met	85	90	95
Arg Ala Arg Gln Gln His Phe Gln Gln Met His Gln Gln Gln Gln Gln	100	105	110
Pro Pro Pro Ala Leu Pro Pro Gly Ser Gln Pro Ile Pro Pro Thr Gly	115	120	125
Ala Ala Gly Pro Pro Ala Xaa His Gly Leu Ala Val Ala Pro Ala Ser	130	135	140
Val Val Pro Ala Pro Ala Gly Ser Gly Ala Pro Pro Gly Ser Leu Gly	145	150	155
Pro Ser Glu Gln Ile Gly Gln Ala Gly Ser Thr Ala Gly Pro Gln Gln	165	170	175
Gln Gln Pro Ala Gly Ala Pro Gln Pro Gly Ala Val Pro Pro Gly Val	180	185	190
Pro Pro Pro Gly Pro His Gly Pro Ser Pro Phe Pro Asn Gln Gln Thr	195	200	205
Pro Pro Ser Met Met Pro Gly Ala Val Pro Gly Ser Gly His Pro Gly	210	215	220
Val Ala Gly Asn Ala Pro Leu Gly Leu Pro Phe Gly Met Pro Pro Pro	225	230	235
Pro Pro Pro Pro Ala Pro Ser Ile Ile Pro Phe Gly Ser Leu Ala Asp	245	250	255
Ser Ile Ser Ile Asn Leu Pro Ala Pro Pro Asn Leu His Gly His His	260	265	270
His His Leu Pro Phe Ala Pro Gly Thr Leu Pro Pro Pro Asn Leu Pro	275	280	285
Val Ser Met Ala Asn Pro Leu His Pro Asn Leu Pro Ala Thr Thr Thr	290	295	300
Met Pro Ser Ser Leu Pro Leu Gly Pro Gly Leu Gly Ser Ala Ala Ala	305	310	315
Gln Ser Pro Ala Ile Val Ala Ala Val Gln Gly Asn Leu Leu Pro Ser	325	330	335
Ala Ser Pro Leu Pro Asp Pro Gly Thr Pro Leu Pro Pro Asp Pro Thr			

462

340                      345                      350  
 Ala Pro Ser Pro Arg His Gly His Pro Cys Xaa His Leu His Ser Glu  
                     355                      360                      365  
 Glu Pro Ala Arg His Leu Ser Pro Ser Pro Pro Val Asp Ile Thr Val  
                     370                      375                      380  
 Pro Gly Thr Ala Leu Pro Pro Pro Leu Gly Pro Ser Pro Ala Trp Arg  
 385                      390                      395                      400  
 Val His His Tyr Val Arg Lys Ala Pro Ser Ala Pro Pro Lys Pro Ser  
                     405                      410                      415  
 Pro Cys Leu Thr Glu Ala Cys Ile Phe Ile Ser Asp Tyr Ser Arg Thr  
                     420                      425                      430  
 Ser Val

<210> 507  
 <211> 303  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (165)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (280)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 507  
 Glu Tyr Val Phe Pro Ala Lys Lys Lys Leu Gln Glu Tyr Arg Val Leu  
                     1                      5                      10                      15  
 Ile Thr Thr Leu Ile Thr Ala Gly Ser Trp Ser Arg Pro Ser Phe Pro  
                     20                      25                      30  
 Leu Ile Thr Ser His Thr Ser Ser Ser Met Arg Leu Ala Thr Ala Trp  
                     35                      40                      45  
 Ser Leu Arg Ser Leu Val Ala Ile Ala Gly Leu Met Glu Val Lys Glu  
                     50                      55                      60  
 Thr Gly Asp Pro Gly Gly Gln Leu Val Leu Ala Gly Asp Pro Arg Gln

463

65		70		75		80
Leu Gly Pro Val Leu Arg Ser Pro Leu Thr Gln Lys His Gly Leu Gly						
	85			90		95
Tyr Ser Leu Leu Glu Arg Leu Leu Thr Tyr Asn Ser Leu Tyr Lys Lys						
	100			105		110
Gly Pro Asp Gly Tyr Asp Pro Gln Phe Ile Thr Lys Leu Leu Arg Asn						
	115			120		125
Tyr Arg Ser His Pro Thr Ile Leu Asp Ile Pro Asn Gln Leu Tyr Tyr						
	130			135		140
Glu Gly Glu Leu Gln Ala Cys Ala Asp Val Val Asp Arg Glu Arg Phe						
	145			150		155
Cys Arg Trp Ala Xaa Leu Pro Arg Gln Gly Phe Pro Ile Ile Phe His						
	165			170		175
Gly Val Met Gly Lys Asp Glu Arg Glu Gly Asn Ser Pro Ser Phe Phe						
	180			185		190
Asn Pro Glu Glu Ala Ala Thr Val Thr Ser Tyr Leu Lys Leu Leu Leu						
	195			200		205
Ala Pro Ser Ser Lys Lys Gly Lys Ala Arg Leu Ser Pro Arg Ser Val						
	210			215		220
Gly Val Ile Ser Pro Tyr Arg Lys Gln Val Glu Lys Ile Arg Tyr Cys						
	225			230		235
Ile Thr Lys Leu Asp Arg Glu Leu Arg Gly Leu Asp Asp Ile Lys Asp						
	245			250		255
Leu Lys Val Gly Ser Val Glu Glu Phe Gln Gly Gln Glu Arg Ser Val						
	260			265		270
Ile Leu Ile Ser Thr Val Arg Xaa Ala Arg Ala Leu Cys Ser Trp Ile						
	275			280		285
Trp Thr Leu Ile Trp Val Ser Leu Arg Thr Pro Arg Gly Ser Met						
	290			295		300

&lt;210&gt; 508

&lt;211&gt; 250

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

464

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (16)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 508

Glu Gln Tyr Leu Pro Leu Thr Glu Glu Glu Leu Glu Lys Glu Ala Xaa  
 1 5 10 15

Lys Val Glu Gly Phe Asp Leu Val Gln Lys Pro Ser Tyr Tyr Val Arg  
 20 25 30

Leu Gly Ser Leu Ser Thr Lys Leu His Ser Arg Ala Tyr Gln Gln Ala  
 35 40 45

Leu Ser Arg Val Lys Glu Ala Lys Gln Lys Ser Gln Gln Thr Ile Ser  
 50 55 60

Gln Leu His Ser Thr Val His Leu Ile Glu Phe Ala Arg Lys Asn Val  
 65 70 75 80

Tyr Ser Ala Asn Gln Lys Ile Gln Asp Ala Gln Asp Lys Leu Tyr Leu  
 85 90 95

Ser Trp Val Glu Trp Lys Arg Ser Ile Gly Tyr Asp Asp Thr Asp Glu  
 100 105 110

Ser His Cys Ala Glu His Ile Glu Ser Arg Thr Leu Ala Ile Ala Arg  
 115 120 125

Asn Leu Thr Gln Gln Leu Gln Thr Thr Cys His Thr Leu Leu Ser Asn  
 130 135 140

Ile Gln Gly Val Pro Gln Asn Ile Gln Asp Gln Ala Lys His Met Gly  
 145 150 155 160

Val Met Ala Gly Asp Ile Tyr Ser Val Phe Arg Asn Ala Ala Ser Phe  
 165 170 175

Lys Glu Val Ser Asp Ser Leu Leu Thr Ser Ser Lys Gly Gln Leu Gln  
 180 185 190

Lys Met Lys Glu Ser Leu Asp Asp Val Met Asp Tyr Leu Val Asn Asn  
 195 200 205

Thr Pro Leu Asn Trp Leu Val Gly Pro Phe Tyr Pro Gln Leu Thr Glu  
 210 215 220

Ser Gln Asn Ala Gln Asp Gln Gly Ala Glu Met Asp Lys Ser Ser Gln  
 225 230 235 240

465

Glu Thr Gln Arg Ser Glu His Lys Thr His  
                   245                  250

&lt;210&gt; 509

&lt;211&gt; 98

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (97)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 509

His Glu Leu Trp Gly Cys Gly Pro Val Thr Pro Arg Arg Thr Ala Pro  
   1                  5                  10                  15

Ser Gly Trp Ala Gln Ala Pro Leu Ser Asp Thr Ala Gln Val Tyr Met  
           20                  25                  30

Glu Leu Gln Gly Leu Val Asp Pro Gln Ile Gln Leu Pro Leu Leu Ala  
       35                  40                  45

Ala Arg Ser Thr Ser Cys Arg Ser Ser Leu Ile Ala Ser Gln Pro Gly  
       50                  55                  60

Pro His Gln Lys Gly Arg Gln Gly Leu Arg Gly Asn Lys Ser Phe Leu  
       65                  70                  75                  80

Pro Ser Ser Trp Asn Cys Gln Asn Trp Thr Arg Gln Pro Leu Thr Ser  
           85                  90                  95

Xaa Ser

&lt;210&gt; 510

&lt;211&gt; 392

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 510

Gly Ala Met Arg Gly Asp Arg Gly Arg Gly Arg Gly Arg Phe Gly  
   1                  5                  10                  15

Ser Arg Gly Gly Pro Gly Gly Gly Phe Arg Pro Phe Val Pro His Ile  
       20                  25                  30

466

Pro Phe Asp Phe Tyr Leu Cys Glu Met Ala Phe Pro Arg Val Lys Pro  
 35 40 45  
 Ala Pro Asp Glu Thr Ser Phe Ser Glu Ala Leu Leu Lys Arg Asn Gln  
 50 55 60  
 Asp Leu Ala Pro Asn Ser Ala Glu Gln Ala Ser Ile Leu Ser Leu Val  
 65 70 75 80  
 Thr Lys Ile Asn Asn Val Ile Asp Asn Leu Ile Val Ala Pro Gly Thr  
 85 90 95  
 Phe Glu Val Gln Ile Glu Glu Val Arg Gln Val Gly Ser Tyr Lys Lys  
 100 105 110  
 Gly Thr Met Thr Thr Gly His Asn Val Ala Asp Leu Val Val Ile Leu  
 115 120 125  
 Lys Ile Leu Pro Thr Leu Glu Ala Val Ala Ala Leu Gly Asn Lys Val  
 130 135 140  
 Val Glu Ser Leu Arg Ala Gln Asp Pro Ser Glu Val Leu Thr Met Leu  
 145 150 155 160  
 Thr Asn Glu Thr Gly Phe Glu Ile Ser Ser Ser Asp Ala Thr Val Lys  
 165 170 175  
 Ile Leu Ile Thr Thr Val Pro Pro Asn Leu Arg Lys Leu Asp Pro Glu  
 180 185 190  
 Leu His Leu Asp Ile Lys Val Leu Gln Ser Ala Leu Ala Ala Ile Arg  
 195 200 205  
 His Ala Arg Trp Phe Glu Glu Asn Ala Ser Gln Ser Thr Val Lys Val  
 210 215 220  
 Leu Ile Arg Leu Leu Lys Asp Leu Arg Ile Arg Phe Pro Gly Phe Glu  
 225 230 235 240  
 Pro Leu Thr Pro Trp Ile Leu Asp Leu Leu Gly His Tyr Ala Val Met  
 245 250 255  
 Asn Asn Pro Thr Arg Gln Pro Leu Ala Leu Asn Val Ala Tyr Arg Arg  
 260 265 270  
 Cys Leu Gln Ile Leu Ala Ala Gly Leu Phe Leu Pro Gly Ser Val Gly  
 275 280 285  
 Ile Thr Asp Pro Cys Glu Ser Gly Asn Phe Arg Val His Thr Val Met  
 290 295 300



467

Thr Leu Glu Gln Gln Asp Met Val Cys Tyr Thr Ala Gln Thr Leu Val  
 305 310 315 320

Arg Ile Leu Ser His Gly Gly Phe Arg Lys Ile Leu Gly Gln Glu Gly  
 325 330 335

Asp Ala Ser Tyr Leu Ala Ser Glu Ile Ser Thr Trp Asp Gly Val Ile  
 340 345 350

Val Thr Pro Ser Glu Lys Ala Tyr Glu Lys Pro Pro Glu Lys Lys Glu  
 355 360 365

Gly Glu Glu Glu Glu Glu Asn Thr Glu Glu Pro Pro Gln Gly Glu Glu  
 370 375 380

Glu Glu Ser Met Glu Thr Gln Glu  
 385 390

&lt;210&gt; 511

&lt;211&gt; 72

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 511

His Gly Gly Gly Lys Gly Arg Gln Val Gly Leu His Ser Val Gln Arg  
 1 5 10 15

Pro Ala Arg Arg Glu Thr Ala Ala Ser Trp Gly Leu Cys Val Lys Ile  
 20 25 30

Pro Asp Leu Gly Val Ala Phe Val Tyr Lys Met Gln Glu Gly Lys Pro  
 35 40 45

Val Pro Asp Ser Ser Arg Gln His Ala Gln Leu Ser Gly Ser Pro Val  
 50 55 60

Ser Gln Gly Leu Ser Leu Pro Leu  
 65 70

&lt;210&gt; 512

&lt;211&gt; 181

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (14)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (33)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (135)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 512

Gly	Trp	Cys	Ser	Cys	Ala	His	Ser	Ser	Ala	Trp	Pro	Gly	Xaa	Trp	Gly
1				5					10					15	

Ala	Ser	Gly	Ile	Pro	Gln	Gln	Ala	Pro	Met	Thr	Val	Cys	Asp	Gln	Ala
			20					25					30		

Xaa	Pro	Val	Thr	Phe	Leu	Leu	Leu	His	Leu	Glu	Gly	Gly	Asp	Ile	His
		35					40					45			

Thr	Val	Ser	His	Leu	Ser	Ser	Pro	Pro	Pro	Gly	Val	Ala	His	Arg	Met
	50					55					60				

Gly	Thr	Gly	Gly	Ser	Arg	Asn	Pro	Asn	Pro	Ala	Trp	Leu	Gly	Gly	Ala
65					70					75					80

Leu	Leu	Val	Arg	Gly	Arg	Pro	Ala	Ser	Leu	Ala	Pro	Trp	Gly	His	Ser
				85					90					95	

Trp	Lys	Arg	Gly	Leu	Ala	His	Ala	Pro	Leu	Arg	Ala	Gly	Thr	Cys	Thr
			100					105					110		

Gly	His	Thr	Arg	His	Ser	Ala	Cys	Trp	Asn	Arg	Trp	Leu	Cys	Ser	Cys
		115					120					125			

Ser	Gly	Pro	Arg	Ala	Ala	Xaa	Leu	Arg	Pro	Cys	Thr	Ser	His	Met	His
	130					135					140				

Trp	Thr	Arg	Ala	Glu	Thr	Pro	Val	Cys	Tyr	Arg	Ala	Leu	Val	Leu	Cys
145					150					155				160	

Gly	Pro	Gly	Ala	Thr	Ala	Gln	Ser	Ser	Gln	Trp	Arg	Ser	Thr	Pro	Leu
				165					170					175	

Asp	Ser	Ile	Phe	Phe
			180	

469

<210> 513  
 <211> 202  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (15)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 513

```

Leu Gly Asp Thr Ile Glu Gly Thr Pro Ala Gly Thr Val Pro Xaa Phe
  1               5               10               15

Pro Gly Arg Pro Thr Arg Ala Ile Met Ala Gln Asp Gln Gly Glu Lys
      20               25               30

Glu Asn Pro Met Arg Glu Leu Arg Ile Arg Lys Leu Cys Leu Asn Ile
      35               40               45

Cys Val Gly Glu Ser Gly Asp Arg Leu Thr Arg Ala Ala Lys Val Leu
      50               55               60

Glu Gln Leu Thr Gly Gln Thr Pro Val Phe Ser Lys Ala Arg Tyr Thr
      65               70               75               80

Val Arg Ser Phe Gly Ile Arg Arg Asn Glu Lys Ile Ala Val His Cys
      85               90               95

Thr Val Arg Gly Ala Lys Ala Glu Glu Ile Leu Glu Lys Gly Leu Lys
      100              105              110

Val Arg Glu Tyr Glu Leu Arg Lys Asn Asn Phe Ser Asp Thr Gly Asn
      115              120              125

Phe Gly Phe Gly Ile Gln Glu His Ile Asp Leu Gly Ile Lys Tyr Asp
      130              135              140

Pro Ser Ile Gly Ile Tyr Gly Leu Asp Phe Tyr Val Val Leu Gly Arg
      145              150              155              160

Pro Gly Phe Ser Ile Ala Asp Lys Lys Arg Arg Thr Gly Cys Ile Gly
      165              170              175

Ala Lys His Arg Ile Ser Lys Glu Glu Ala Met Arg Trp Phe Gln Gln
      180              185              190

Lys Tyr Asp Gly Ile Ile Leu Pro Gly Lys
      195              200

```

470

<210> 514  
<211> 63  
<212> PRT  
<213> Homo sapiens

<220>  
<221> SITE  
<222> (1)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (2)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (5)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (16)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (35)  
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 514  
Xaa Xaa Lys Asn Xaa Ile Thr Pro Lys Glu Glu Ser Pro Pro His Xaa  
1 5 10 15  
Ala Leu Leu Ser Lys Cys Leu Leu Thr Pro Ser Pro Lys Met Pro Pro  
20 25 30  
Ile Leu Xaa Val Met Ala Ala Leu Gly Phe Glu Arg Arg Glu Phe Gly  
35 40 45  
Ser Thr Ser Val Glu Arg Val Gln Ser Arg Gln Leu Asp Cys Phe  
50 55 60

<210> 515  
<211> 218  
<212> PRT  
<213> Homo sapiens

471

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (151)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (209)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (211)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 515

Ser	Leu	Ala	Arg	Gly	Cys	Gln	Arg	Pro	Asp	Ala	Val	Leu	Tyr	Ala	Arg
1				5					10					15	

His	Tyr	Asn	Ile	Pro	Val	Ile	His	Ala	Phe	Arg	Arg	Ala	Val	Asp	Asp
		20					25						30		

Pro	Gly	Leu	Val	Phe	Asn	Gln	Leu	Pro	Lys	Met	Leu	Tyr	Pro	Glu	Tyr
	35					40						45			

His	Lys	Val	His	Gln	Met	Met	Arg	Glu	Gln	Ser	Ile	Leu	Ser	Pro	Ser
	50					55					60				

Pro	Tyr	Glu	Gly	Tyr	Arg	Ser	Leu	Pro	Arg	His	Gln	Leu	Leu	Cys	Phe
65					70					75				80	

Lys	Glu	Asp	Cys	Gln	Ala	Val	Phe	Gln	Asp	Leu	Glu	Gly	Val	Glu	Lys
			85						90					95	

Val	Phe	Gly	Val	Ser	Leu	Val	Leu	Val	Leu	Ile	Gly	Ser	His	Pro	Asp
		100					105						110		

Leu	Ser	Phe	Leu	Pro	Gly	Ala	Gly	Ala	Asp	Phe	Ala	Val	Asp	Pro	Asp
	115						120						125		

Gln	Pro	Leu	Ser	Ala	Lys	Arg	Asn	Pro	Ile	Asp	Val	Asp	Pro	Phe	Thr
	130					135					140				

Tyr	Gln	Ser	Thr	Arg	Gln	Xaa	Gly	Leu	Tyr	Ala	Met	Gly	Pro	Leu	Ala
145					150					155				160	

Gly	Asp	Asn	Phe	Val	Arg	Phe	Val	Gln	Gly	Gly	Ala	Leu	Ala	Val	Ala
			165						170					175	

Ser	Ser	Leu	Leu	Arg	Lys	Glu	Gln	Asn	His	Leu	His	Arg	Gln	Pro	Trp
		180						185						190	

472

Ser Ser Leu Arg Gly Ile His Pro Leu Ile Asp Leu Lys Ser Gly Val  
195 200 205

Xaa Pro Xaa Leu Val Lys Leu Thr Ala Gln  
210 215

&lt;210&gt; 516

&lt;211&gt; 41

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (22)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 516

Asn Gly Arg Pro Asp Ser Thr Gly Pro Ala Ile Pro Gly Ile Leu Ser  
1 5 10 15

Trp Gly Phe Glu Thr Xaa Leu Arg Asp Arg Glu Thr Asp Pro Arg Asn  
20 25 30

Val Leu Asn Cys Asn Gly Pro His Thr  
35 40

&lt;210&gt; 517

&lt;211&gt; 250

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (118)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (161)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (204)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys  
245 250

474

<210> 518  
 <211> 100  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (3)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (7)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 518  
 Asn Pro Xaa Lys Lys Leu Xaa Ile Leu Ile Lys Trp Pro Pro Pro Phe  
   1                  5                  10                  15  
 Pro Pro Ser Phe Pro Pro Ser Pro Asn Ser Leu Ser Ser Ser Ser Phe  
                   20                  25                  30  
 Pro Pro Pro Leu Ser Leu Phe Ser Pro Ser Phe Thr Phe Leu Ile Ser  
           35                  40                  45  
 Val Lys Leu Glu Arg Phe Glu Ile Pro Ile Lys Val Arg Leu Ser Pro  
   50                  55                  60  
 Glu Pro Trp Thr Pro Glu Thr Gly Leu Val Thr Asp Ala Phe Lys Leu  
   65                  70                  75                  80  
 Lys Arg Lys Glu Leu Arg Asn His Tyr Leu Lys Asp Ile Glu Arg Met  
                   85                  90                  95  
 Tyr Gly Gly Lys  
           100

<210> 519  
 <211> 60  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (5)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE



475

&lt;222&gt; (17)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 519

His Glu Asp Gly Xaa Leu Met Gly Cys Arg His Arg Trp His Pro Arg  
 1 5 10 15

Xaa Val Pro Phe His Gln Thr Ser Pro Lys Thr Glu Leu Glu Ser Thr  
 20 25 30

Ile Phe Gly Ser Pro Arg Leu Ala Ser Gly Leu Phe Pro Glu Trp Gln  
 35 40 45

Ser Trp Gly Arg Met Glu Asn Leu Ala Ser Tyr Arg  
 50 55 60

&lt;210&gt; 520

&lt;211&gt; 120

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (25)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 520

Ser His Pro Tyr Ala Pro Ser Cys Gly Leu Arg Gly Pro Gly Ala Ala  
 1 5 10 15

Ser Arg Ala Arg Thr Arg Glu Arg Xaa Pro Gln Ala Glu Ala Glu Ala  
 20 25 30

Arg Ser Thr Pro Gly Pro Ala Gly Ser Arg Leu Gly Pro Glu Thr Phe  
 35 40 45

Arg Gln Arg Phe Arg Gln Phe Arg Tyr Gln Asp Ala Ala Gly Pro Arg  
 50 55 60

Glu Ala Phe Arg Gln Leu Arg Glu Leu Ser Arg Gln Trp Leu Arg Pro  
 65 70 75 80

Asp Ile Arg Thr Lys Glu Gln Ile Val Glu Met Leu Val Gln Glu Gln  
 85 90 95

Leu Leu Ala Ile Leu Pro Glu Ala Ala Arg Ala Arg Arg Ile Arg Arg  
 100 105 110

Arg Thr Asp Val Arg Ile Thr Gly

476

115

120

&lt;210&gt; 521

&lt;211&gt; 96

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 521

Gly His Gln Thr Val Ser Pro Ser Thr Gly Ser Arg Val Thr Arg Met  
 1 5 10 15

Phe Ser Leu Ile Ser Phe Ser His Val Phe Ile Lys Asp Ile Cys Lys  
 20 25 30

Leu Pro Lys Asp Glu Gly Thr Cys Arg Asp Phe Ile Leu Lys Trp Tyr  
 35 40 45

Tyr Asp Pro Asn Thr Lys Ser Cys Ala Arg Phe Trp Tyr Gly Gly Cys  
 50 55 60

Gly Gly Asn Glu Asn Lys Phe Gly Ser Gln Lys Glu Cys Glu Lys Val  
 65 70 75 80

Cys Ala Pro Val Leu Ala Lys Pro Gly Val Ile Ser Val Met Gly Thr  
 85 90 95

&lt;210&gt; 522

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (18)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 522

Asn Ser Gly Phe Arg Pro Lys Asn Pro Val Gly Arg Gly Gly Glu Pro  
 1 5 10 15

Glu Xaa Cys Gly Gly Ala Gly Gly Leu Gly Cys Thr Leu Val Trp Gly  
 20 25 30

Gly Thr Gly Ala Ala Val Val Thr Gly Val Val Trp Leu Leu Leu Pro

477

35                      40                      45  
 Asn Gly Gly Val Gly Val Gly Leu Leu Gly Pro Gln Ser Pro Val Gly  
     50                      55                      60  
 Gly Ser Asp Ser Ala Pro Tyr Ser Leu His Pro Ala Gly Arg Thr Trp  
     65                      70                      75                      80  
 Gly Leu Arg Ser Glu Cys Ile Pro Pro Leu Ser Phe Asn Leu Ser Cys  
                     85                      90                      95  
 Arg Thr His Ser Gly Pro Gly Ala Arg Leu Gly Glu Ala Gly Pro Asn  
                     100                      105                      110  
 Tyr Gly Ser Arg Glu Leu Gln Val Pro Thr  
                     115                      120

&lt;210&gt; 523

&lt;211&gt; 94

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 523

Leu Ile Pro Gln Val Cys Cys Lys His Ser Met Glu Asp Thr Asp Asp  
     1                      5                      10                      15  
 Ser Leu Val Leu Val Phe Leu Ser Ala Val Asn Val Gln Gln Phe Ala  
                     20                      25                      30  
 Gln Glu Leu Gly Asp His Ile Cys Leu Ser Gly Gln Gly Ser Glu Val  
                     35                      40                      45  
 His Trp Asn Leu Leu Arg Asn Leu Phe Val Lys Thr Ile Val Asn Asn  
                     50                      55                      60  
 Tyr Cys Ile Phe Leu Gln Lys Tyr Ile Leu Glu Asn Cys Ile Leu Ser  
                     65                      70                      75                      80  
 Ile Lys Val Phe Leu Cys Lys Lys Lys Lys Lys Lys Leu Val  
                     85                      90

&lt;210&gt; 524

&lt;211&gt; 93

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (78)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (86)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (93)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 524

Ser	Ala	Val	Met	Gly	Arg	Lys	Lys	Lys	Lys	Gln	Leu	Lys	Pro	Trp	Cys
1				5					10					15	

Trp	Tyr	Cys	Asn	Arg	Asp	Phe	Asp	Asp	Glu	Lys	Ile	Leu	Ile	Gln	His
			20					25					30		

Gln	Lys	Ala	Lys	His	Phe	Lys	Cys	His	Ile	Cys	His	Lys	Lys	Leu	Tyr
		35					40					45			

Thr	Gly	Pro	Gly	Leu	Ala	Ile	His	Cys	Met	Gln	Val	His	Lys	Glu	Thr
	50					55					60				

Ile	Asp	Ala	Val	Pro	Asn	Ala	Tyr	Leu	Gly	Glu	Gln	Thr	Xaa	Ile	Gly
65					70					75					80

Asn	Ile	Trp	Tyr	Gly	Xaa	Tyr	Ser	Arg	Lys	Arg	Tyr	Xaa
				85					90			

&lt;210&gt; 525

&lt;211&gt; 324

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (323)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 525

Asp	Leu	Arg	Leu	Ser	Arg	Pro	Glu	Ala	Val	Glu	Ala	Glu	Ala	Met	Met
1				5					10					15	

Ala	Ala	Met	Ala	Thr	Ala	Arg	Val	Arg	Met	Gly	Pro	Arg	Cys	Ala	Gln
			20					25					30		

Ala Leu Trp Arg Met Pro Trp Leu Pro Val Phe Leu Ser Leu Ala Ala  
 35 40 45  
 Ala Ala Ala Ala Ala Ala Ala Glu Gln Gln Val Pro Leu Val Leu Trp  
 50 55 60  
 Ser Ser Asp Arg Asp Leu Trp Ala Pro Ala Ala Asp Thr His Glu Gly  
 65 70 75 80  
 His Ile Thr Ser Asp Leu Gln Leu Ser Thr Tyr Leu Asp Pro Ala Leu  
 85 90 95  
 Glu Leu Gly Pro Arg Asn Val Leu Leu Phe Leu Gln Asp Lys Leu Ser  
 100 105 110  
 Ile Glu Asp Phe Thr Ala Tyr Gly Gly Val Phe Gly Asn Lys Gln Asp  
 115 120 125  
 Ser Ala Phe Ser Asn Leu Glu Asn Ala Leu Asp Leu Ala Pro Ser Ser  
 130 135 140  
 Leu Val Leu Pro Ala Val Asp Trp Tyr Ala Val Ser Thr Leu Thr Thr  
 145 150 155 160  
 Tyr Leu Gln Glu Lys Leu Gly Ala Ser Pro Leu His Val Asp Leu Ala  
 165 170 175  
 Thr Leu Arg Glu Leu Lys Leu Asn Ala Ser Leu Pro Ala Leu Leu Leu  
 180 185 190  
 Ile Arg Leu Pro Tyr Thr Ala Ser Ser Gly Leu Met Ala Pro Arg Glu  
 195 200 205  
 Val Leu Thr Gly Asn Asp Glu Val Ile Gly Gln Val Leu Ser Thr Leu  
 210 215 220  
 Lys Ser Glu Asp Val Pro Tyr Thr Ala Ala Leu Thr Ala Val Arg Pro  
 225 230 235 240  
 Ser Arg Val Ala Arg Asp Val Ala Val Val Ala Gly Gly Leu Gly Arg  
 245 250 255  
 Gln Leu Leu Gln Lys Gln Pro Val Ser Pro Val Ile His Pro Pro Val  
 260 265 270  
 Ser Tyr Asn Asp Thr Ala Pro Arg Ile Leu Phe Trp Ala Gln Asn Phe  
 275 280 285  
 Ser Val Ala Tyr Lys Asp Gln Trp Glu Asp Leu Thr Pro Leu Thr Phe  
 290 295 300

480

Gly Val Gln Glu Leu Asn Leu Thr Gly Ser Phe Trp Asn Asp Ser Phe  
 305 310 315 320

Ala Ser Xaa His

<210> 526

<211> 66

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (2)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 526

Phe Xaa Val Ser Trp Thr Trp Lys Gln Val Ser Glu Phe Pro Gly Asp  
 1 5 10 15

Gln Arg Asp Glu Val Leu Gln Leu Pro Pro Ser Ser Cys Asn Leu Val  
 20 25 30

Ser Ser Gly Ala Gly Gly Glu Pro Glu Lys Leu Ala Ser Tyr Ile Thr  
 35 40 45

Ser Leu Trp Leu Phe Phe Ile Cys Lys Thr Arg Ile Ile Leu Asn Cys  
 50 55 60

Lys Gly  
 65

<210> 527

<211> 62

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (40)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 527

Asn Thr Gln Leu Trp Phe Leu Cys Phe Pro Asn Cys Lys Ala Ala Asp  
 1 5 10 15

481

Asn Lys Thr Pro Gly Phe His Val Ser Ser Ala Met Ser Thr Leu Thr  
                   20                  25                  30  
 Gln Ile Leu Lys Gln Asn Ser Xaa Asn Ala Val Leu Arg Ile Gln Leu  
                   35                  40                  45  
 Leu Leu Lys Pro Ile Ser Ile Cys Ile Ile Thr Thr Asn Ile  
                   50                  55                  60

&lt;210&gt; 528

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (80)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (104)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (105)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 528

Tyr Asn Lys Ile Glu Ile Met His Leu Val Met Trp Pro Thr Ser Leu  
           1                  5                  10                  15  
 Leu Thr Thr Met Asp Cys Phe Gln Gln Gln Leu Ile Phe Trp Ser Val  
                   20                  25                  30  
 Leu Arg Gly Ala Cys Met Ser Phe Val Thr Ser Gly Ser Thr Pro Ala  
                   35                  40                  45  
 Val Lys Tyr Cys Phe His Leu Pro Leu Gln Lys Ala Ser Cys Leu Leu  
                   50                  55                  60  
 Thr Ser Thr Ala Lys Ala Leu Phe Trp Thr Gly Tyr Leu Ile Lys Xaa  
           65                  70                  75                  80  
 Ile Ser Val Arg Leu Cys Ser Val Ile Pro Ser Glu Pro Arg Phe Val  
                   85                  90                  95  
 Ser Lys Ala Thr Val Leu Ser Xaa Xaa Pro Cys Val Trp Gly Gln Val

482

100	105	110
Ala Ile Pro Pro Met Ser Leu Val Ile Leu		
115	120	
<210> 529		
<211> 182		
<212> PRT		
<213> Homo sapiens		
<220>		
<221> SITE		
<222> (25)		
<223> Xaa equals any of the naturally occurring L-amino acids		
<400> 529		
Asp Arg Thr Arg Leu Ser Gln Ala Ser Thr Pro Thr Pro Val Cys Trp		
1	5	10 15
Gly Leu Leu Gln Pro Pro Pro Trp Xaa Glu Ala Trp Tyr Arg Leu Thr		
20	25	30
His Arg Gly Leu Cys Gln Val Arg Phe Cys Arg Trp Ser Gln Ala Leu		
35	40	45
Pro Glu Ala Arg Gly Gly Ala Trp Ala Gly Ser Pro Gly Glu Gly Gln		
50	55	60
Ala Gly Pro Arg Leu His Thr His Ile Gln Pro Ala Gly Leu Ser Ala		
65	70	75 80
Val Leu Ser Pro Ser Leu Ser Ser Pro Ser Ser Ala Val Thr Leu Ser		
85	90	95
Ser Pro Ser Leu Pro Ala Ser Pro Pro Ala Ala Pro Pro Val Lys Arg		
100	105	110
Met Thr Lys Asp Leu Ser Tyr Ala Gly Ser Lys Asn Gln Asn Phe Leu		
115	120	125
Leu Ala Phe Ser Phe Val Ala Ser Pro Ala Pro Ala Leu Pro Val Ser		
130	135	140
His Pro Gly Pro Arg Leu Glu Ala Ser Leu His Leu Ser Tyr Cys Phe		
145	150	155 160
Lys Pro Lys Phe Thr Val Ser Val Gly Gly Gln Asp Leu Leu Ser Pro		
165	170	175



483

Pro Leu Leu His Pro Pro  
180

<210> 530

<211> 183

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (79)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (80)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (81)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 530

Ala Leu Val Leu Gly Xaa Lys Ser Val Arg Met Ala Ser Ser Arg Met  
1 5 10 15

Thr Arg Arg Asp Pro Leu Thr Asn Lys Val Ala Leu Val Thr Ala Ser  
20 25 30

Thr Asp Gly Ile Gly Phe Ala Ser Pro Gly Val Trp Pro Arg Thr Gly  
35 40 45

Pro Arg Gly Arg Gln Gln Pro Glu Ala Ala Glu Cys Gly Pro Gly Gly  
50 55 60

Gly Thr Leu Gln Gly Glu Gly Leu Ser Val Thr Gly Thr Cys Xaa Xaa  
65 70 75 80

Xaa Gly Lys Ala Glu Asp Arg Glu Arg Leu Val Ala Thr Ala Val Lys  
85 90 95

Leu His Gly Gly Ile Asp Ile Leu Val Ser Asn Ala Ala Val Asn Pro  
100 105 110

484

[illegible]

<210> 531

<211> 129

<212> PRT

<213> Homo sapiens

**<220>**

**<221> SITE**

<222> (89)

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

<221> SITE

$\langle 222 \rangle$  (103)

<222> Xaa equals any of the naturally occurring L-amino acids

<400> 531

Asn	Ser	Ala	Pro	Leu	Ser	Thr	Gly	Leu	Gly	Gln	Gly	His	Thr	Gly	
1				5				10					15		
His	Val	Arg	Phe	Leu	Ala	Ala	Val	Gln	Leu	Pro	Asp	Gly	Phe	Asn	Leu
			20					25					30		
Leu	Cys	Pro	Thr	Pro	Pro	Pro	Pro	Pro	Asp	Thr	Gly	Pro	Glu	Lys	Leu
			35					40					45		
Pro	Ser	Leu	Glu	His	Arg	Asp	Ser	Pro	Trp	His	Arg	Gly	Pro	Ala	Pro
			50				55				60				
Ala	Arg	Pro	Lys	Met	Leu	Val	Ile	Ser	Gly	Gly	Asp	Gly	Tyr	Glu	Asp
65					70					75					80
Phe	Arg	Leu	Ser	Ser	Gly	Gly	Gly	Xaa	Ala	Val	Arg	Leu	Trp	Val	Glu
					85				90					95	

485

Thr Thr Ala Gln Thr Thr Xaa Ser Cys Gly Gly Cys Asp Pro Val Cys  
 100 105 110

Arg Gly Pro Gly Leu Ala Arg Pro Pro Ala Phe Ser Leu Leu Ala Ser  
 115 120 125

Pro

<210> 532

<211> 91

<212> PRT

<213> Homo sapiens

<400> 532

Gly Ala Ile Ala Ser Ser Gly Pro Thr Gly Gly Arg Val Arg Lys His  
 1 5 10 15

Gln Leu Leu Pro Gly Ala Val Arg Glu Trp Glu Gln Leu Trp Ala Pro  
 20 25 30

His Phe Arg Gln Val Leu Pro Lys Pro Ser Asp Ala Val Arg Pro Gly  
 35 40 45

Leu Pro Val Val Leu Phe Arg Leu Cys Phe Gln Asn Ala Phe Ile Ser  
 50 55 60

Ser Val Pro Phe Gly Pro His Lys Ser Pro Trp Gly Val Gly Gly Gly  
 65 70 75 80

Leu Cys Arg His Pro His Phe Lys Ala Gly Ser  
 85 90

<210> 533

<211> 67

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (63)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 533

Asn Leu Cys Gln Val Gln Pro Thr Arg Leu Tyr Ser Ser Leu His Ser  
 1 5 10 15

486

Gly Leu His His Val Arg Gln Val Thr Gln Lys Ser Tyr Lys Val Ser  
                     20                    25                    30  
 Thr Ser Gly Pro Arg Ala Phe Ser Ser Arg Ser Tyr Thr Ser Gly Pro  
                     35                    40                    45  
 Gly Ser Arg Ile Ser Ser Ser Ala Phe Ser Arg Val Gly Gly Xaa Ser  
                     50                    55                    60  
 Gly Gly Ala  
                     65

<210> 534  
 <211> 144  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (140)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (141)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 534  
 Phe Asn Arg Arg Tyr Pro Lys Ile Gln Phe Ser Leu Ser Thr Gly Pro  
                     1                    5                    10                    15  
 Ser Gly Thr Met Leu Asp Gly Val Leu Glu Gly Lys Leu Asn Ala Ala  
                     20                    25                    30  
 Phe Ile Asp Gly Pro Ile Asn His Thr Ala Ile Asp Gly Ile Pro Val  
                     35                    40                    45  
 Tyr Arg Glu Glu Leu Met Ile Val Thr Pro Gln Gly Tyr Ala Pro Val  
                     50                    55                    60  
 Thr Arg Ala Ser Gln Val Asn Gly Ser Asn Ile Tyr Ala Phe Arg Ala  
                     65                    70                    75                    80  
 Asn Cys Ser Tyr Arg Arg His Phe Glu Ser Trp Phe His Ala Asp Gly  
                     85                    90                    95  
 Ala Ala Pro Gly Thr Ile His Glu Met Glu Ser Tyr His Gly Met Leu  
                     100                    105                    110

487

Ala Cys Val Ile Ala Gly Ala Gly Ile Ala Leu Ile Pro Arg Ser Met  
 115 120 125

Leu Glu Ser Met Pro Gly His His Gln Val Glu Xaa Xaa Ala Val Ser  
 130 135 140

&lt;210&gt; 535

&lt;211&gt; 175

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 535

Arg Ala Pro Ala Arg Ile Ser Gly Gly Gly Ser Ala Met Val Gly Gly  
 1 5 10 15

Gly Gly Val Gly Gly Gly Leu Leu Glu Asn Ala Asn Pro Leu Ile Tyr  
 20 25 30

Gln Arg Ser Gly Glu Arg Pro Val Thr Ala Gly Glu Glu Asp Glu Gln  
 35 40 45

Val Pro Asp Ser Ile Asp Ala Arg Glu Ile Phe Asp Leu Ile Arg Ser  
 50 55 60

Ile Asn Asp Pro Glu His Pro Leu Thr Leu Glu Glu Leu Asn Val Val  
 65 70 75 80

Glu Gln Val Arg Val Gln Val Ser Asp Pro Glu Ser Thr Val Ala Val  
 85 90 95

Ala Phe Thr Pro Thr Ile Pro His Cys Ser Met Ala Thr Leu Ile Gly  
 100 105 110

Leu Ser Ile Lys Val Lys Leu Leu Arg Ser Leu Pro Gln Arg Phe Lys  
 115 120 125

Met Asp Val His Ile Thr Pro Gly Thr His Ala Ser Glu His Ala Val  
 130 135 140

Asn Lys Gln Leu Ala Asp Lys Glu Arg Val Ala Ala Ala Leu Glu Asn  
 145 150 155 160

Thr His Leu Leu Glu Val Val Asn Gln Cys Leu Ser Ala Arg Ser  
 165 170 175

488

&lt;210&gt; 536

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 536

Gly Trp His Arg Thr His His Arg Gly Arg His Gln Ala Arg Glu Ala  
1 5 10 15

Glu Glu Glu Ala Trp Ala Ala Ala Glu Pro Ile Lys Lys Val Arg Lys  
20 25 30

Ser Leu Ala Leu Asp Ile Val Asp Glu Asp Val Lys Leu Met Met Ser  
35 40 45

Thr Leu Pro Lys Ser Leu Ser Leu Pro Thr Thr Ala Pro Ser Asn Ser  
50 55 60

Ser Ser Leu Thr Leu Ser Gly Ile Lys Glu Asp Asn Ser Leu Leu Asn  
65 70 75 80

Gln Gly Phe Leu Gln Ala Lys Pro Glu Lys Ala Ala Val Ala Gln Lys  
85 90 95

Pro Arg Ser His Phe Thr Thr Pro Ala Pro Met Ser Ser Ala Trp Lys  
100 105 110

Thr Val Ala Cys Gly Gly Thr Arg Asp Gln Leu Phe Met Gln Glu Lys  
115 120 125

Ala Arg Gln Leu Leu Gly Arg Leu Lys Pro Ser His Thr Ser Arg Thr  
130 135 140

Leu Ile Leu Ser  
145

&lt;210&gt; 537

&lt;211&gt; 70

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (41)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

489

<221> SITE

<222> (42)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 537

Arg	Pro	Thr	Arg	Ser	Ala	Trp	Trp	Gly	Arg	Leu	Leu	Ser	Arg	Val	Ser
1				5					10					15	

Pro Gln Pro Arg Pro Ala Ser Pro Ser Val Ser Thr Arg Asn Gln Leu  
20 25 30

Pro Glu Ala Arg Arg Gly Val Glu Xaa Xaa Glu Cys Glu Glu Thr Ala  
35 40 45

Ala Ser Ala Glu Arg Ala Gly Pro Pro Arg Ala Leu Val Phe Gly Ala  
50 55 60

Gln Ser Arg Ser Pro Gly  
65 70

<210> 538

<211> 206

<212> PRT

<213> Homo sapiens

<400> 538

Gly Glu Val Ser Ala Ser Gly Ile Ala Arg Arg Gly Gly Pro Met Ala  
1 5 10 15

Pro Leu Gly Gly Ala Pro Arg Leu Val Leu Leu Phe Ser Gly Lys Arg  
20 25 30

Lys Ser Gly Lys Asp Phe Val Thr Glu Ala Leu Gln Ser Arg Leu Gly  
35 40 45

Ala Asp Val Cys Ala Val Leu Arg Leu Ser Gly Pro Leu Lys Glu Gln  
50 55 60

Tyr Ala Gln Glu His Gly Leu Asn Phe Gln Arg Leu Leu Asp Thr Ser  
65 70 75 80

Thr Tyr Lys Glu Ala Phe Arg Lys Asp Met Ile Arg Trp Gly Glu Glu  
85 90 95

Lys Arg Gln Ala Asp Pro Gly Phe Phe Cys Arg Lys Ile Val Glu Gly  
100 105 110

Ile Ser Gln Pro Ile Trp Leu Val Ser Asp Thr Arg Arg Val Ser Asp  
115 120 125

490

Ile Gln Trp Phe Arg Glu Ala Tyr Gly Ala Val Thr Gln Thr Val Arg  
 130 135 140

Val Val Ala Leu Glu Gln Ser Arg Gln Gln Arg Gly Trp Val Phe Thr  
 145 150 155 160

Pro Gly Val Asp Asp Ala Glu Ser Glu Cys Gly Leu Asp Asn Phe Gly  
 165 170 175

Asp Phe Asp Trp Val Ile Glu Asn His Gly Val Glu Gln Arg Leu Glu  
 180 185 190

Glu Gln Leu Glu Asn Leu Ile Glu Phe Ile Arg Ser Arg Leu  
 195 200 205

&lt;210&gt; 539

&lt;211&gt; 350

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 539

Ser Thr Leu Ile Ala Phe Ile Val Ile Ser Thr Leu Phe Pro Leu Leu  
 1 5 10 15

Asp Met Thr Glu Ile Tyr Phe Ser Leu Leu Asp Glu Ile Val Asp Thr  
 20 25 30

Leu Gly Glu Gly Ala Phe Gly Lys Val Val Glu Cys Ile Asp His Lys  
 35 40 45

Ala Gly Gly Arg His Val Ala Val Lys Ile Val Lys Asn Val Asp Arg  
 50 55 60

Tyr Cys Glu Ala Ala Arg Ser Glu Ile Gln Val Leu Glu His Leu Asn  
 65 70 75 80

Thr Thr Asp Pro Asn Ser Thr Phe Arg Cys Val Gln Met Leu Glu Trp  
 85 90 95

Phe Glu His His Gly His Ile Cys Ile Val Phe Glu Leu Leu Gly Leu  
 100 105 110

Ser Thr Tyr Asp Phe Ile Lys Glu Asn Gly Phe Leu Pro Phe Arg Leu  
 115 120 125

Asp His Ile Arg Lys Met Ala Tyr Gln Ile Cys Lys Ser Val Asn Phe  
 130 135 140



491

Leu His Ser Asn Lys Leu Thr His Thr Asp Leu Lys Pro Glu Asn Ile  
 145 150 155 160  
 Leu Phe Val Gln Ser Asp Tyr Thr Glu Ala Tyr Asn Pro Lys Ile Lys  
 165 170 175  
 Arg Asp Glu Arg Thr Leu Ile Asn Pro Asp Ile Lys Val Val Asp Phe  
 180 185 190  
 Gly Ser Ala Thr Tyr Asp Asp Glu His His Ser Thr Leu Val Ser Thr  
 195 200 205  
 Arg His Tyr Arg Ala Pro Glu Val Ile Leu Ala Leu Gly Trp Ser Gln  
 210 215 220  
 Pro Cys Asp Val Trp Ser Ile Gly Cys Ile Leu Ile Glu Tyr Tyr Leu  
 225 230 235 240  
 Gly Phe Thr Val Phe Pro Thr His Asp Ser Lys Glu His Leu Ala Met  
 245 250 255  
 Met Glu Arg Ile Leu Gly Pro Leu Pro Lys His Met Ile Gln Lys Thr  
 260 265 270  
 Arg Lys Arg Lys Tyr Phe His His Asp Arg Leu Asp Trp Asp Glu His  
 275 280 285  
 Ser Ser Ala Gly Arg Tyr Val Ser Arg Arg Cys Lys Pro Leu Lys Glu  
 290 295 300  
 Phe Met Leu Ser Gln Asp Val Glu His Glu Arg Leu Phe Asp Leu Ile  
 305 310 315 320  
 Gln Lys Met Leu Glu Tyr Asp Pro Ala Lys Arg Ile Thr Leu Arg Glu  
 325 330 335  
 Ala Leu Lys His Pro Phe Phe Asp Leu Leu Lys Lys Ser Ile  
 340 345 350

&lt;210&gt; 540

&lt;211&gt; 324

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (54)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (56)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (297)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (304)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (305)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (317)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (321)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 540  
 Gln Ala Thr Met Gly Asn Val Leu Ala Ala Ser Ser Pro Pro Ala Gly  
 1 5 10 15  
 Pro Pro Pro Pro Pro Ala Pro Ala Leu Val Gly Leu Pro Pro Pro Pro  
 20 25 30  
 Pro Ser Pro Pro Gly Phe Thr Leu Pro Pro Leu Gly Gly Ser Leu Gly  
 35 40 45  
 Ala Gly Thr Ser Thr Xaa Arg Xaa Ser Glu Arg Thr Pro Gly Ala Ala  
 50 55 60  
 Thr Ala Ser Ala Ser Gly Ala Ala Glu Asp Gly Ala Cys Gly Cys Leu  
 65 70 75 80  
 Pro Asn Pro Gly Thr Phe Glu Glu Cys His Arg Lys Cys Lys Glu Leu  
 85 90 95  
 Phe Pro Ile Gln Met Glu Gly Val Lys Leu Thr Val Asn Lys Gly Leu  
 100 105 110

493

Ser Asn His Phe Gln Val Asn His Thr Val Ala Leu Ser Thr Ile Gly  
 115 120 125  
 Glu Ser Asn Tyr His Phe Gly Val Thr Tyr Val Gly Thr Lys Gln Leu  
 130 135 140  
 Ser Pro Thr Glu Ala Phe Pro Val Leu Val Gly Asp Met Asp Asn Ser  
 145 150 155 160  
 Gly Ser Leu Asn Ala Gln Val Ile His Gln Leu Gly Pro Gly Leu Arg  
 165 170 175  
 Ser Lys Met Ala Ile Gln Thr Gln Gln Ser Lys Phe Val Asn Trp Gln  
 180 185 190  
 Val Asp Gly Glu Tyr Arg Gly Ser Asp Phe Thr Ala Ala Val Thr Leu  
 195 200 205  
 Gly Asn Pro Asp Val Leu Val Gly Ser Gly Ile Leu Val Ala His Tyr  
 210 215 220  
 Leu Gln Ser Ile Thr Pro Cys Leu Ala Leu Gly Gly Glu Leu Val Tyr  
 225 230 235 240  
 His Arg Arg Pro Gly Glu Glu Gly Thr Val Met Ser Leu Ala Gly Lys  
 245 250 255  
 Tyr Thr Leu Asn Asn Trp Leu Ala Thr Val Thr Leu Gly Gln Ala Gly  
 260 265 270  
 Met His Ala Thr Tyr Tyr His Lys Ala Ser Asp Gln Leu Gln Val Gly  
 275 280 285  
 Val Glu Phe Glu Ala Ser Thr Arg Xaa Gln Asp Thr Ser Val Ser Xaa  
 290 295 300  
 Xaa Val Pro Ala Trp Asn Leu Pro Lys Gly Gln Pro Xaa Leu Ser Lys  
 305 310 315 320  
 Xaa Leu Leu Gly

&lt;210&gt; 541

&lt;211&gt; 204

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 541

494

```

Arg Gly Pro Thr Phe Thr Pro Glu Ile Met Ala Ala Glu Asp Val Val
 1           5           10           15

Ala Thr Gly Ala Asp Pro Ser Asp Leu Glu Ser Gly Gly Leu Leu His
      20           25           30

Glu Ile Phe Thr Ser Pro Leu Asn Leu Leu Leu Gly Leu Cys Ile
      35           40           45

Phe Leu Leu Tyr Lys Ile Val Arg Gly Asp Gln Pro Ala Ala Ser Gly
      50           55           60

Asp Ser Asp Asp Asp Glu Pro Pro Pro Leu Pro Arg Leu Lys Arg Arg
      65           70           75           80

Asp Phe Thr Pro Ala Glu Leu Arg Arg Phe Asp Gly Val Gln Asp Pro
      85           90           95

Arg Ile Leu Met Ala Ile Asn Gly Lys Val Phe Asp Val Thr Lys Gly
      100          105          110

Arg Lys Phe Tyr Gly Pro Glu Gly Pro Tyr Gly Val Phe Ala Gly Arg
      115          120          125

Asp Ala Ser Arg Gly Leu Ala Thr Phe Cys Leu Asp Lys Glu Ala Leu
      130          135          140

Lys Asp Glu Tyr Asp Asp Leu Ser Asp Leu Thr Ala Ala Gln Gln Glu
      145          150          155          160

Thr Leu Ser Asp Trp Glu Ser Gln Phe Thr Phe Lys Tyr His His Val
      165          170          175

Gly Lys Leu Leu Lys Glu Gly Glu Glu Pro Thr Val Tyr Ser Asp Glu
      180          185          190

Glu Glu Pro Lys Asp Glu Ser Ala Arg Lys Asn Asp
      195          200

```

&lt;210&gt; 542

&lt;211&gt; 193

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (183)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

495

&lt;400&gt; 542

Pro Ala Tyr Ser Leu Gly Leu Leu Lys Ser Val Leu Asp Gly Gly Gly  
 1 5 10 15

Ala Gly Ala His Gln Ala Arg Ser Asn Pro Ser Cys Met Tyr Pro Gln  
 20 25 30

Gly Thr Phe Val Ile Pro Leu Leu Val Thr Ala His Arg Asp Pro Thr  
 35 40 45

Gln Phe Lys Asp Pro Asp Cys Phe Asn Pro Thr Asn Phe Leu Asp Lys  
 50 55 60

Gly Lys Phe Gln Gly Asn Asp Ala Phe Met Pro Phe Ala Ser Gly Ala  
 65 70 75 80

Gly Arg Gly Gly Arg Gly Pro Ala Trp Thr Gly Ser Gly Val Pro Gly  
 85 90 95

Ala His Cys Ala Pro Val Tyr Pro Ala Lys Gln Met Cys Leu Gly Thr  
 100 105 110

Gly Leu Ala His Ser Gly Ile Phe Leu Phe Leu Thr Ala Thr Leu Gln  
 115 120 125

Arg Phe Cys Leu Leu Pro Val Val Arg Pro Gly Thr Ile Asn Leu Thr  
 130 135 140

Cys Ser Ala Leu Ala Trp Ala Val Ser Pro Gln Thr Ser Ser Ser Ser  
 145 150 155 160

Gln Trp Pro Ala Glu Val Arg Leu His Tyr Gly Gly Leu Thr Gly Pro  
 165 170 175

Gln Thr Ser Ile Pro Ser Xaa Val Asn Lys Gly Pro Lys Leu Gln Lys  
 180 185 190

Lys

&lt;210&gt; 543

&lt;211&gt; 352

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (5)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (154)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (167)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 543

Ser Thr Val Arg Xaa Pro Gly Arg Pro Thr Arg Pro Met Ala Ala Glu  
 1 5 10 15

Glu Pro Gln Gln Gln Lys Gln Glu Pro Leu Gly Ser Asp Ser Glu Val  
 20 25 30

Leu Thr Val Trp Pro Met Met Lys Pro Ser Trp Leu Ser Arg Thr Glu  
 35 40 45

Phe Ser Lys Arg Leu Leu Cys Arg Thr Leu Trp Cys Gln Ser Gly Trp  
 50 55 60

Ser Ser Arg Ser Tyr Thr Arg Ser Met Leu Lys Met Thr Thr Ser Ile  
 65 70 75 80

Asn Arg Arg Ser Arg Thr Ser Thr Lys Ser Thr Arg Thr Ser Ala Arg  
 85 90 95

Pro Gly Leu Thr Ala Thr Val Ser Ile Gly Leu Ser Asp Ser Pro Thr  
 100 105 110

Trp Arg His Cys Trp Met Thr Ala Arg Ser Cys Ser Gly Glu Lys Gly  
 115 120 125

Gly His Trp Ala Pro Arg Gln Val Gly Val Tyr Leu Leu Pro Gly Arg  
 130 135 140

Val Gly Cys Val Ser Ser Arg Val Ser Xaa Ser Phe Pro Gly Asp Gly  
 145 150 155 160

Leu Asp Ser Gly Leu Ala Xaa Arg Gly Ser Ala Val Ser Ala Leu Ala  
 165 170 175

Ser Gly Leu Val Glu Glu Pro Met Leu Gly Pro Pro Phe His Pro Thr  
 180 185 190

Pro Arg Phe Lys Ala Val Ser Ala Lys Ser Lys Glu Asp Leu Val Ser  
 195 200 205

497

Gln Gly Phe Thr Glu Phe Thr Ile Glu Asp Phe His Asn Thr Phe Met  
 210 215 220  
 Asp Leu Ile Glu Gln Val Glu Lys Gln Thr Ser Val Ala Asp Leu Leu  
 225 230 235 240  
 Ala Ser Phe Asn Asp Gln Ser Thr Ser Asp Tyr Leu Val Val Tyr Leu  
 245 250 255  
 Arg Leu Leu Thr Ser Gly Tyr Leu Gln Arg Glu Ser Lys Phe Phe Glu  
 260 265 270  
 His Phe Ile Glu Gly Gly Arg Thr Val Lys Glu Phe Cys Gln Gln Glu  
 275 280 285  
 Val Glu Pro Met Cys Lys Glu Ser Asp His Ile His Ile Ile Ala Leu  
 290 295 300  
 Ala Gln Ala Leu Ser Val Ser Ile Gln Val Glu Tyr Met Asp Arg Gly  
 305 310 315 320  
 Glu Gly Gly Thr Thr Asn Pro His Ile Phe Pro Glu Gly Ser Glu Pro  
 325 330 335  
 Lys Val Tyr Leu Leu Tyr Arg Pro Gly His Tyr Asp Ile Leu Tyr Lys  
 340 345 350

&lt;210&gt; 544

&lt;211&gt; 240

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 544

Ser Thr His Ala Ser Glu Met Ala Glu Arg Gly Tyr Ser Phe Ser Leu  
 1 5 10 15  
 Thr Thr Phe Ser Pro Ser Gly Lys Leu Val Gln Ile Glu Tyr Ala Leu  
 20 25 30  
 Ala Ala Val Ala Gly Gly Ala Pro Ser Val Gly Ile Lys Ala Ala Asn  
 35 40 45  
 Gly Val Val Leu Ala Thr Glu Lys Lys Gln Lys Ser Ile Leu Tyr Asp  
 50 55 60  
 Glu Arg Ser Val His Lys Val Glu Pro Ile Thr Lys His Ile Gly Leu

498

```

65              70              75              80
Val Tyr Ser Gly Met Gly Pro Asp Tyr Arg Val Leu Val His Arg Ala
      85              90              95
Arg Lys Leu Ala Gln Gln Tyr Tyr Leu Val Tyr Gln Glu Pro Ile Pro
      100             105             110
Thr Ala Gln Leu Val Gln Arg Val Ala Ser Val Met Gln Glu Tyr Thr
      115             120             125
Gln Ser Gly Gly Val Arg Pro Phe Gly Val Ser Leu Leu Ile Cys Gly
      130             135             140
Trp Asn Glu Gly Arg Pro Tyr Leu Phe Gln Ser Asp Pro Ser Gly Ala
      145             150             155             160
Tyr Phe Ala Trp Lys Ala Thr Ala Met Gly Lys Asn Tyr Val Asn Gly
      165             170             175
Lys Thr Phe Leu Glu Lys Arg Tyr Asn Glu Asp Leu Glu Leu Glu Asp
      180             185             190
Ala Ile His Thr Ala Ile Leu Thr Leu Lys Glu Ser Phe Glu Gly Gln
      195             200             205
Met Thr Glu Asp Asn Ile Glu Val Gly Ile Cys Asn Glu Ala Gly Phe
      210             215             220
Arg Arg Leu Thr Pro Thr Glu Val Lys Asp Tyr Leu Ala Ala Ile Ala
      225             230             235             240

```

&lt;210&gt; 545

&lt;211&gt; 181

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 545

```

Arg Cys Ile Leu Tyr Thr Gly Phe Met Leu Gly Ala Gln Arg Glu Val
  1              5              10              15
Asp Ser Arg Leu Leu Ala Leu Pro Gly Arg Lys Val Pro Thr Ser Trp
      20              25              30
Trp Asp Asp Leu Phe Lys Gly Ala Lys Glu His Gly Ala Val Ala Val
      35              40              45

```



499

Glu Arg Val Thr Lys Ser Pro Gly Glu Thr Ser Lys Pro Arg Pro Phe  
 50 55 60  
 Ala Gly Gly Gly Tyr Arg Leu Gly Ala Ala Pro Glu Glu Glu Ser Ala  
 65 70 75 80  
 Tyr Val Ala Gly Glu Lys Arg Gln His Ser Ser Gln Asp Val His Val  
 85 90 95  
 Val Leu Lys Leu Trp Lys Ser Gly Phe Ser Leu Asp Asn Gly Glu Leu  
 100 105 110  
 Arg Ser Tyr Gln Asp Pro Ser Asn Ala Gln Phe Leu Glu Ser Ile Arg  
 115 120 125  
 Arg Gly Glu Val Pro Ala Glu Leu Arg Arg Leu Ala His Gly Gly Gln  
 130 135 140  
 Val Asn Leu Asp Met Glu Asp His Arg Asp Glu Asp Phe Val Lys Pro  
 145 150 155 160  
 Lys Gly Ala Phe Lys Ala Phe Thr Gly Glu Gly Gln Lys Leu Gly Ser  
 165 170 175  
 Thr Ala Pro Arg Cys  
 180

&lt;210&gt; 546

&lt;211&gt; 197

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 546

Pro Arg Val Arg Arg Arg Ala Arg Ala Ala Ala Gly Ser Ser His Ala  
 1 5 10 15  
 Ala Met Ala Asp Ser Glu Leu Gln Leu Val Glu Gln Arg Ile Arg Ser  
 20 25 30  
 Phe Pro Asp Phe Pro Thr Pro Gly Val Val Phe Arg Asp Ile Ser Pro  
 35 40 45  
 Val Leu Lys Asp Pro Ala Ser Phe Arg Ala Ala Ile Gly Leu Leu Ala  
 50 55 60  
 Arg His Leu Lys Ala Thr His Gly Gly Arg Ile Asp Tyr Ile Ala Gly  
 65 70 75 80

500

Leu Asp Ser Arg Gly Phe Leu Phe Gly Pro Ser Leu Ala Gln Glu Leu  
                     85                    90                    95  
 Gly Leu Gly Cys Val Leu Ile Arg Lys Arg Gly Lys Leu Pro Gly Pro  
                     100                    105                    110  
 Thr Leu Trp Ala Ser Tyr Ser Leu Glu Tyr Gly Lys Ala Glu Leu Glu  
                     115                    120                    125  
 Ile Gln Lys Asp Ala Leu Glu Pro Gly Gln Arg Val Val Val Val Asp  
                     130                    135                    140  
 Asp Leu Leu Ala Thr Gly Gly Thr Met Asn Ala Ala Cys Glu Leu Leu  
                     145                    150                    155                    160  
 Gly Arg Leu Gln Ala Glu Val Leu Glu Cys Val Ser Leu Val Glu Leu  
                     165                    170                    175  
 Thr Ser Leu Lys Gly Arg Glu Lys Leu Ala Pro Val Pro Phe Phe Ser  
                     180                    185                    190  
 Leu Leu Gln Tyr Glu  
                     195

&lt;210&gt; 547

&lt;211&gt; 93

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (84)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 547

Glu Thr Gly Lys Glu Ser Lys Ala Leu Phe Leu Pro Phe Pro Gly Ser  
           1                    5                    10                    15  
 Val Tyr Ser Thr Ser Thr Gly Glu Ala Ser Gly Glu Gly Leu Ser Pro  
                     20                    25                    30  
 Leu Pro His Leu His Glu Phe Trp Asn Ser Val Leu Leu Ala Ala Cys  
                     35                    40                    45  
 Phe Gln Leu Pro Pro Ile Ser Ile Ala Ala Gly Ser Ser Cys Leu Phe  
                     50                    55                    60  
 Tyr Ser Val Ile Lys His Pro Ala Pro Thr Leu Ser Gln Arg Ser Ile  
                     65                    70                    75                    80

501

Leu Ile Leu Xaa Lys Lys Ile Tyr Glu Glu Lys Lys Lys  
                     85                    90

&lt;210&gt; 548

&lt;211&gt; 49

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (5)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 548

Gly Leu Gln Leu Xaa Ala His Ala Ala Gly Arg Val Pro Gly Cys Ala  
   1                    5                    10                    15

Leu Gln Gly Leu Gly His Phe Leu Gln Glu Asn Lys Gln Leu Leu Arg  
                     20                    25                    30

Asp Val Leu Ala Gln Glu Leu His Lys Pro Ala Phe Glu Gly Arg His  
                     35                    40                    45

Ile

&lt;210&gt; 549

&lt;211&gt; 379

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 549

Val Ala Cys Cys Val Arg Ile Pro Gly Pro Pro Arg Arg Ser Gly Pro  
   1                    5                    10                    15

Ala Met Ala Val Thr Ile Thr Leu Lys Thr Leu Gln Gln Gln Thr Phe  
                     20                    25                    30

Lys Ile Arg Met Glu Pro Asp Glu Thr Val Lys Val Leu Lys Glu Lys  
                     35                    40                    45

Ile Glu Ala Glu Lys Gly Arg Asp Ala Phe Pro Val Ala Gly Gln Lys  
                     50                    55                    60

Leu Ile Tyr Ala Gly Lys Ile Leu Ser Asp Asp Val Pro Ile Arg Asp  
   65                    70                    75                    80

Tyr Arg Ile Asp Glu Lys Asn Phe Val Val Val Met Val Thr Lys Thr  
 85 90 95  
 Lys Ala Gly Gln Gly Thr Ser Ala Pro Pro Glu Ala Ser Pro Thr Ala  
 100 105 110  
 Ala Pro Glu Ser Ser Thr Ser Phe Pro Pro Ala Pro Thr Ser Gly Met  
 115 120 125  
 Ser His Pro Pro Pro Ala Ala Arg Glu Asp Lys Ser Pro Ser Glu Glu  
 130 135 140  
 Ser Ala Pro Thr Thr Ser Pro Glu Ser Val Ser Gly Ser Val Pro Ser  
 145 150 155 160  
 Ser Gly Ser Ser Gly Arg Glu Glu Asp Ala Ala Ser Thr Leu Val Thr  
 165 170 175  
 Gly Ser Glu Tyr Glu Thr Met Leu Thr Glu Ile Met Ser Met Gly Tyr  
 180 185 190  
 Glu Arg Glu Arg Val Val Ala Ala Leu Arg Ala Ser Tyr Asn Asn Pro  
 195 200 205  
 His Arg Ala Val Glu Tyr Leu Leu Thr Gly Ile Pro Gly Ser Pro Glu  
 210 215 220  
 Pro Glu His Gly Ser Val Gln Glu Ser Gln Val Ser Glu Gln Pro Ala  
 225 230 235 240  
 Thr Glu Ala Gly Glu Asn Pro Leu Glu Phe Leu Arg Asp Gln Pro Gln  
 245 250 255  
 Phe Gln Asn Met Arg Gln Val Ile Gln Gln Asn Pro Ala Leu Leu Pro  
 260 265 270  
 Ala Leu Leu Gln Gln Leu Gly Gln Glu Asn Pro Gln Leu Leu Gln Gln  
 275 280 285  
 Ile Ser Arg His Gln Glu Gln Phe Ile Gln Met Leu Asn Glu Pro Pro  
 290 295 300  
 Gly Glu Leu Ala Asp Ile Ser Asp Val Glu Gly Glu Val Gly Ala Ile  
 305 310 315 320  
 Gly Glu Glu Ala Pro Gln Met Asn Tyr Ile Gln Val Thr Pro Gln Glu  
 325 330 335  
 Lys Glu Ala Ile Glu Arg Leu Lys Ala Leu Gly Phe Pro Glu Ser Leu  
 340 345 350

503

Val Ile Gln Ala Tyr Phe Ala Cys Glu Lys Asn Glu Asn Leu Ala Ala  
355 360 365

Asn Phe Leu Leu Ser Gln Asn Phe Asp Asp Glu  
370 375

<210> 550

<211> 275

<212> PRT

<213> Homo sapiens

**<220>**

**<221> SITE**

<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

<221> SITE

**<222> (235)**

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

**<222> (260)**

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

<221> SITE

**<222> (261)**

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

**<221> SITE**

**<222> (267)**

<223> Xaa equals any of the naturally occurring L-amino acids

**<220>**

<221> SITE

$\langle 222 \rangle$  (272)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 550

Cys Ser Cys Lys Arg Xaa His Gln Gln Gln Val Leu Pro Pro Arg Gln  
1 5 10 15

Pro Ser Ala Leu Val Pro Ser Val Thr Glu Tyr Arg Leu Asp Gly His  
20 25 30

504

Thr Ile Ser Asp Leu Ser Arg Ser Ser Arg Gly Glu Leu Ile Pro Ile  
 35 40 45  
 Ser Pro Ser Thr Glu Val Gly Gly Ser Gly Ile Gly Thr Pro Pro Ser  
 50 55 60  
 Val Leu Lys Arg Gln Arg Lys Arg Arg Val Ala Leu Ser Pro Val Thr  
 65 70 75 80  
 Glu Asn Ser Thr Ser Leu Ser Phe Leu Asp Ser Cys Asn Ser Leu Thr  
 85 90 95  
 Pro Lys Ser Thr Pro Val Lys Thr Leu Pro Phe Ser Pro Ser Gln Phe  
 100 105 110  
 Leu Asn Phe Trp Asn Lys Gln Asp Thr Leu Glu Leu Glu Ser Pro Ser  
 115 120 125  
 Leu Thr Ser Thr Pro Val Cys Ser Gln Lys Val Val Val Thr Thr Pro  
 130 135 140  
 Leu His Arg Asp Lys Thr Pro Leu His Gln Lys His Ala Ala Phe Val  
 145 150 155 160  
 Thr Pro Asp Gln Lys Tyr Ser Met Asp Asn Thr Pro His Thr Pro Thr  
 165 170 175  
 Pro Phe Lys Asn Ala Leu Glu Lys Tyr Gly Pro Leu Lys Pro Leu Pro  
 180 185 190  
 Gln Thr Pro His Leu Glu Glu Asp Leu Lys Glu Val Leu Arg Ser Glu  
 195 200 205  
 Ala Gly Ile Glu Leu Ile Ile Glu Asp Asp Ile Arg Pro Glu Lys Gln  
 210 215 220  
 Lys Arg Lys Pro Gly Leu Arg Arg Ser Pro Xaa Lys Lys Val Arg Lys  
 225 230 235 240  
 Ser Leu Ala Leu Asp Ile Val Asp Glu Asp Val Lys Leu Met Met Ser  
 245 250 255  
 Thr Leu Pro Xaa Xaa Leu Ser Leu Ala Thr Xaa Ala Pro Cys Lys Xaa  
 260 265 270  
 Phe Gln Pro  
 275

&lt;210&gt; 551

505

&lt;211&gt; 161

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (158)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 551

Asn Leu Ala Ala Ala Ser Gly Gly Gly Pro Gln Ser Val Ser Gly Thr  
 1 5 10 15

Leu Leu Cys Glu Pro Val Leu Thr Met Phe Ala Thr Ser Gly Ala Val  
 20 25 30

Ala Ala Gly Lys Pro Tyr Ser Cys Ser Glu Cys Gly Lys Ser Phe Cys  
 35 40 45

Tyr Ser Ser Val Leu Leu Arg His Glu Arg Ala His Gly Gly Asp Gly  
 50 55 60

Arg Phe Arg Cys Leu Glu Cys Gly Glu Arg Cys Ala Arg Ala Ala Asp  
 65 70 75 80

Leu Arg Ala His Arg Arg Thr His Ala Gly Gln Thr Leu Tyr Ile Cys  
 85 90 95

Ser Glu Cys Gly Gln Ser Phe Arg His Ser Gly Arg Leu Asp Leu His  
 100 105 110

Leu Gly Ala His Arg Gln Arg Cys Arg Thr Cys Pro Cys Arg Thr Cys  
 115 120 125

Gly Arg Arg Phe Pro His Leu Pro Ala Leu Leu Leu His Arg Arg Arg  
 130 135 140

Gln His Leu Pro Glu Arg Pro Arg Arg Cys Pro Leu Cys Xaa Leu Arg  
 145 150 155 160

Phe

&lt;210&gt; 552

&lt;211&gt; 405

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 552

506

Pro Arg Val Arg Arg Arg Ala Arg Gly Arg Arg Val Arg Pro Ala Gly  
 1 5 10 15  
 Gly Pro Val Arg Arg Gly Ala Ala Val Arg Gly Ala Leu Arg Gly Ala  
 20 25 30  
 Ser Leu Gly His Gly Ala Ala Ala Arg Ala Gly Arg Pro Leu Cys Val  
 35 40 45  
 Arg His Ser Glu Pro Val Cys Gly Ser Asp Ala Asn Thr Tyr Ala Asn  
 50 55 60  
 Leu Cys Gln Leu Arg Ala Ala Ser Arg Arg Ser Glu Arg Leu His Arg  
 65 70 75 80  
 Pro Pro Val Ile Val Leu Gln Arg Gly Ala Cys Gly Gln Gly Gln Glu  
 85 90 95  
 Asp Pro Asn Ser Leu Arg His Lys Tyr Asn Phe Ile Ala Asp Val Val  
 100 105 110  
 Glu Lys Ile Ala Pro Ala Val Val His Ile Glu Leu Phe Arg Lys Leu  
 115 120 125  
 Pro Phe Ser Lys Arg Glu Val Pro Val Ala Ser Gly Ser Gly Phe Ile  
 130 135 140  
 Val Ser Glu Asp Gly Leu Ile Val Thr Asn Ala His Val Val Thr Asn  
 145 150 155 160  
 Lys His Arg Val Lys Val Glu Leu Lys Asn Gly Ala Thr Tyr Glu Ala  
 165 170 175  
 Lys Ile Lys Asp Val Asp Glu Lys Ala Asp Ile Ala Leu Ile Lys Ile  
 180 185 190  
 Asp His Gln Gly Lys Leu Pro Val Leu Leu Leu Gly Arg Ser Ser Glu  
 195 200 205  
 Leu Arg Pro Gly Glu Phe Val Val Ala Ile Gly Ser Pro Phe Ser Leu  
 210 215 220  
 Gln Asn Thr Val Thr Thr Gly Ile Val Ser Thr Thr Gln Arg Gly Gly  
 225 230 235 240  
 Lys Glu Leu Gly Leu Arg Asn Ser Asp Met Asp Tyr Ile Gln Thr Asp  
 245 250 255  
 Ala Ile Ile Asn Tyr Gly Asn Ser Gly Gly Pro Leu Val Asn Leu Asp  
 260 265 270



507

Gly Glu Val Ile Gly Ile Asn Thr Leu Lys Val Thr Ala Gly Ile Ser  
           275                          280                          285  
 Phe Ala Ile Pro Ser Asp Lys Ile Lys Lys Phe Leu Thr Glu Ser His  
           290                          295                          300  
 Asp Arg Gln Ala Lys Gly Lys Ala Ile Thr Lys Lys Lys Tyr Ile Gly  
 305                          310                          315                          320  
 Ile Arg Met Met Ser Leu Thr Ser Ser Lys Ala Lys Glu Leu Lys Asp  
                           325                          330                          335  
 Arg His Arg Asp Phe Pro Asp Val Ile Ser Gly Ala Tyr Ile Ile Glu  
                           340                          345                          350  
 Val Ile Pro Asp Thr Pro Ala Glu Ala Gly Gly Leu Lys Glu Asn Asp  
           355                          360                          365  
 Val Ile Ile Ser Ile Asn Gly Gln Ser Val Val Ser Ala Asn Asp Val  
           370                          375                          380  
 Ser Asp Val Ile Lys Arg Glu Ser Thr Leu Asn Met Val Val Arg Arg  
 385                          390                          395                          400  
 Val Met Lys Ile Ser  
                           405

&lt;210&gt; 553

&lt;211&gt; 107

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 553

Ala Gln Glu Asn Glu Glu Met Glu Gln Pro Met Gln Asn Gly Glu Glu  
   1                          5                          10                          15  
 Asp Arg Pro Leu Gly Gly Gly Glu Gly His Gln Pro Ala Gly Asn Arg  
           20                          25                          30  
 Arg Gly Gln Ala Arg Arg Leu Ala Pro Asn Phe Arg Trp Ala Ile Pro  
           35                          40                          45  
 Asn Arg Gln Ile Asn Asp Gly Met Gly Gly Asp Gly Asp Asp Met Glu  
           50                          55                          60  
 Ile Phe Met Glu Glu Met Arg Glu Ile Arg Arg Lys Leu Arg Glu Leu  
   65                          70                          75                          80  
 Gln Leu Arg Asn Cys Leu Arg Ile Leu Met Gly Glu Leu Ser Asn His

508

	85	90	95
His Asp His His Asp Glu Phe Cys Leu Met Pro			
100	105		

<210> 554  
 <211> 229  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (8)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (15)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (20)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (27)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (78)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 554  
 Gly Leu Ser Ala Glu Ser Thr Xaa Thr Ser Thr Met Pro Met Xaa Leu  
 1 5 10 15  
 Gly Tyr Trp Xaa Ile Arg Gly Leu Ala His Xaa Ile Arg Leu Leu Leu  
 20 25 30  
 Glu Tyr Thr Asp Ser Ser Tyr Glu Glu Lys Lys Tyr Thr Met Gly Asp  
 35 40 45  
 Ala Pro Asp Tyr Asp Arg Ser Gln Trp Leu Asn Glu Lys Phe Lys Leu  
 50 55 60  
 Gly Leu Asp Phe Pro Asn Leu Pro Tyr Leu Ile Asp Gly Xaa His Lys

509

```

65              70              75              80
Ile Thr Gln Ser Asn Ala Ile Leu Arg Tyr Ile Ala Arg Lys His Asn
      85              90              95
Leu Cys Gly Glu Ser Glu Lys Glu Gln Ile Arg Glu Asp Ile Leu Glu
      100             105             110
Asn Gln Phe Met Asp Ser Arg Met Gln Leu Ala Lys Leu Cys Tyr Asp
      115             120             125
Pro Asp Phe Glu Lys Leu Lys Pro Glu Tyr Leu Gln Ala Leu Pro Glu
      130             135             140
Met Leu Lys Leu Tyr Ser Gln Phe Leu Gly Lys Gln Pro Trp Phe Leu
      145             150             155             160
Gly Asp Lys Ile Thr Phe Val Asp Phe Ile Ala Tyr Asp Val Leu Glu
      165             170             175
Arg Asn Gln Val Phe Glu Pro Ser Cys Leu Asp Ala Phe Pro Asn Leu
      180             185             190
Lys Asp Phe Ile Ser Arg Phe Glu Gly Leu Glu Lys Ile Ser Ala Tyr
      195             200             205
Met Lys Ser Ser Arg Phe Leu Pro Arg Pro Val Phe Thr Lys Met Ala
      210             215             220
Val Trp Gly Asn Lys
225

```

&lt;210&gt; 555

&lt;211&gt; 106

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (59)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (60)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

510

&lt;222&gt; (72)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (98)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 555

Asn Val Ile Ser Val Asp Pro Asn Asp Gln Lys Lys Thr Ala Cys Tyr  
 1 5 10 15

Asp Ile Asp Val Glu Val Asp Asp Thr Leu Lys Thr Gln Met Asn Ser  
 20 25 30

Phe Leu Leu Ser Thr Ala Ser Gln Gln Glu Ile Ala Thr Leu Asp Asn  
 35 40 45

Lys Thr Met Thr Asp Val Val Gly Asn Gln Xaa Xaa Ser Ala Glu Leu  
 50 55 60

Ser Ser Thr Ser Ser Pro Gly Xaa Gly Gly Cys Val Pro Ile Leu Leu  
 65 70 75 80

Leu Gln Gly Ala Ala Glu Thr Thr Arg Ile Arg Ala Ser Pro Gly Asn  
 85 90 95

Pro Xaa Tyr Ile Gly Pro Leu Pro Gln Pro  
 100 105

&lt;210&gt; 556

&lt;211&gt; 86

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 556

Gly Arg Ala Thr Lys Gln Asn Thr Thr Lys Pro Asn His Arg Ile Ile  
 1 5 10 15

Phe Asn Pro Thr Phe Tyr Thr Met Pro Gln Phe Pro Ile Thr Leu His  
 20 25 30

Thr Ser Phe Cys Val Gln Leu Asn Cys Asn Cys Phe Leu Tyr Leu Glu  
 35 40 45

Arg Val Thr Ile Glu Leu Glu Thr Phe Tyr Ser Gly Arg Leu Gly Ser  
 50 55 60

Phe Trp Trp Asp Ser Val Gly Glu Arg Glu Glu Gly Glu Val Gly Gly

```

65              70              75              80
Leu Leu Pro Phe Arg Thr
      85

.

<210> 557
<211> 565
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (57)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (71)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (75)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (82)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (118)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (120)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (552)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 557
Ala Ser Leu Thr Gly Thr Gln Ala Leu Pro Pro Leu Phe Ser Leu Gly
  1              5              10              15

```

512

Tyr His Gln Ser Arg Trp Asn Tyr Arg Asp Glu Ala Asp Val Leu Glu  
 20 25 30  
 Val Asp Gln Gly Phe Asp Asp His Asn Leu Pro Cys Asp Val Ile Trp  
 35 40 45  
 Leu Asp Ile Glu His Ala Asp Gly Xaa Arg Tyr Phe Thr Trp Asp Pro  
 50 55 60  
 Ser Arg Phe Pro Gln Pro Xaa Thr Met Leu Xaa Arg Leu Ala Ser Lys  
 65 70 75 80  
 Arg Xaa Lys Leu Val Ala Ile Val Asp Pro His Ile Lys Val Asp Ser  
 85 90 95  
 Gly Tyr Arg Val His Glu Glu Leu Arg Asn Leu Gly Leu Tyr Val Lys  
 100 105 110  
 Thr Arg Asp Gly Ser Xaa Tyr Xaa Gly Trp Cys Trp Pro Gly Ser Ala  
 115 120 125  
 Gly Tyr Pro Asp Phe Thr Asn Pro Thr Met Arg Ala Trp Trp Ala Asn  
 130 135 140  
 Met Phe Ser Tyr Asp Asn Tyr Glu Gly Ser Ala Pro Asn Leu Phe Val  
 145 150 155 160  
 Trp Asn Asp Met Asn Glu Pro Ser Val Phe Asn Gly Pro Glu Val Thr  
 165 170 175  
 Met Leu Lys Asp Ala Gln His Tyr Gly Gly Trp Glu His Arg Asp Val  
 180 185 190  
 His Asn Ile Tyr Gly Leu Tyr Val His Met Ala Thr Ala Asp Gly Leu  
 195 200 205  
 Arg Gln Arg Ser Gly Gly Met Glu Arg Pro Phe Val Leu Ala Arg Ala  
 210 215 220  
 Phe Phe Ala Gly Ser Gln Arg Phe Gly Ala Val Trp Thr Gly Asp Asn  
 225 230 235 240  
 Thr Ala Glu Trp Asp His Leu Lys Ile Ser Ile Pro Met Cys Leu Ser  
 245 250 255  
 Leu Gly Leu Val Gly Leu Ser Phe Cys Gly Ala Asp Val Gly Gly Phe  
 260 265 270  
 Phe Lys Asn Pro Glu Pro Glu Leu Leu Val Arg Trp Tyr Gln Met Gly  
 275 280 285

513

Ala Tyr Gln Pro Phe Phe Arg Ala His Ala His Leu Asp Thr Gly Arg  
 290 295 300  
 Arg Glu Pro Trp Leu Leu Pro Ser Gln His Asn Asp Ile Ile Arg Asp  
 305 310 315 320  
 Ala Leu Gly Gln Arg Tyr Ser Leu Leu Pro Phe Trp Tyr Thr Leu Leu  
 325 330 335  
 Tyr Gln Ala His Arg Glu Gly Ile Pro Val Met Arg Pro Leu Trp Val  
 340 345 350  
 Gln Tyr Pro Gln Asp Val Thr Thr Phe Asn Ile Asp Asp Gln Tyr Leu  
 355 360 365  
 Leu Gly Asp Ala Leu Leu Val His Pro Val Ser Asp Ser Gly Ala His  
 370 375 380  
 Gly Val Gln Val Tyr Leu Pro Gly Gln Gly Glu Val Trp Tyr Asp Ile  
 385 390 395 400  
 Gln Ser Tyr Gln Lys His His Gly Pro Gln Thr Leu Tyr Leu Pro Val  
 405 410 415  
 Thr Leu Ser Ser Ile Pro Val Phe Gln Arg Gly Gly Thr Ile Val Pro  
 420 425 430  
 Arg Trp Met Arg Val Arg Arg Ser Ser Glu Cys Met Lys Asp Asp Pro  
 435 440 445  
 Ile Thr Leu Phe Val Ala Leu Ser Pro Gln Gly Thr Ala Gln Gly Glu  
 450 455 460  
 Leu Phe Leu Asp Asp Gly His Thr Phe Asn Tyr Gln Thr Arg Gln Glu  
 465 470 475 480  
 Phe Leu Leu Arg Arg Phe Ser Phe Ser Gly Asn Thr Leu Val Ser Ser  
 485 490 495  
 Ser Ala Asp Pro Glu Gly His Phe Glu Thr Pro Ile Trp Ile Glu Arg  
 500 505 510  
 Val Val Ile Ile Gly Ala Gly Lys Pro Ala Ala Val Val Leu Gln Thr  
 515 520 525  
 Lys Gly Ser Pro Glu Ser Arg Leu Ser Phe Gln His Asp Pro Glu Thr  
 530 535 540  
 Ser Val Leu Val Leu Arg Lys Xaa Gly Ile Asn Val Ala Ser Asp Trp  
 545 550 555 560

514

Ser Ile His Leu Arg  
565

&lt;210&gt; 558

&lt;211&gt; 160

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (39)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 558

Arg Glu Ala Val Leu Pro Gln Ala Val Leu Arg His Pro Val Arg Thr  
1 5 10 15

Gln Arg Arg Glu His Arg Gly Arg Gly Leu Leu His Leu Arg Glu Ala  
20 25 30

Pro Gly Gly Gly Ala Ala Xaa His Arg Pro His Arg Gly Pro Arg Gly  
35 40 45

Pro Ser Arg Gly Ala Glu Gly Glu Arg Pro Pro Glu Gly Pro Ser Arg  
50 55 60

Ala Ser Ser Val Thr Thr Phe Thr Gly Glu Pro Asn Thr Cys Pro Arg  
65 70 75 80

Cys Ser Lys Lys Val Tyr Phe Ala Glu Lys Val Thr Ser Leu Gly Lys  
85 90 95

Asp Trp His Arg Pro Cys Leu Arg Cys Glu Arg Cys Gly Lys Thr Leu  
100 105 110

Thr Pro Gly Gly His Ala Glu His Asp Gly Gln Pro Tyr Cys His Lys  
115 120 125

Pro Cys Tyr Gly Ile Leu Phe Gly Pro Lys Gly Val Asn Thr Gly Ala  
130 135 140

Val Gly Ser Tyr Ile Tyr Asp Arg Asp Pro Glu Gly Lys Val Gln Pro  
145 150 155 160



515

&lt;210&gt; 559

&lt;211&gt; 480

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 559

Gly Cys Ile Gly Tyr Leu Val Leu Leu Trp Pro Leu Pro Leu Ile His  
 1 5 10 15

Phe Gly Leu Ala Asn Gln Ser Glu Asp Leu Ser Val Phe Tyr Pro Gly  
 20 25 30

Thr Leu Leu Glu Thr Gly His Asp Ile Leu Phe Phe Trp Val Ala Arg  
 35 40 45

Met Val Met Leu Gly Leu Lys Leu Thr Gly Arg Leu Pro Phe Arg Glu  
 50 55 60

Val Tyr Leu His Ala Ile Val Arg Asp Ala His Gly Arg Lys Met Ser  
 65 70 75 80

Lys Ser Leu Gly Asn Val Ile Asp Pro Leu Asp Val Ile Tyr Gly Ile  
 85 90 95

Ser Leu Gln Gly Leu His Asn Gln Leu Leu Asn Ser Asn Leu Asp Pro  
 100 105 110

Ser Glu Val Glu Lys Ala Lys Glu Gly Gln Lys Ala Asp Phe Pro Ala  
 115 120 125

Gly Ile Pro Glu Cys Gly Thr Asp Ala Leu Arg Phe Gly Leu Cys Ala  
 130 135 140

Tyr Met Ser Gln Gly Arg Asp Ile Asn Leu Asp Val Asn Arg Ile Leu  
 145 150 155 160

Gly Tyr Arg His Phe Cys Asn Lys Leu Trp Asn Ala Thr Lys Phe Ala  
 165 170 175

Leu Arg Gly Leu Gly Lys Gly Phe Val Pro Ser Pro Thr Ser Gln Pro  
 180 185 190

Gly Gly His Glu Ser Leu Val Asp Arg Trp Ile Arg Ser Arg Leu Thr  
 195 200 205

Glu Ala Val Arg Leu Ser Asn Gln Gly Phe Gln Ala Tyr Asp Phe Pro  
 210 215 220

Ala Val Thr Thr Ala Gln Tyr Ser Phe Trp Leu Tyr Glu Leu Cys Asp  
 225 230 235 240

516

Val Tyr Leu Glu Cys Leu Lys Pro Val Leu Asn Gly Val Asp Gln Val  
245 250 255

Ala Ala Glu Cys Ala Arg Gln Thr Leu Tyr Thr Cys Leu Asp Val Gly  
260 265 270

Leu Arg Leu Leu Ser Pro Phe Met Pro Phe Val Thr Glu Glu Leu Phe  
275 280 285

Gln Arg Leu Pro Arg Arg Met Pro Gln Ala Pro Pro Ser Leu Cys Val  
290 295 300

Thr Pro Tyr Pro Glu Pro Ser Glu Cys Ser Trp Lys Asp Pro Glu Ala  
305 310 315 320

Glu Ala Ala Leu Glu Leu Ala Leu Ser Ile Thr Arg Ala Val Arg Ser  
325 330 335

Leu Arg Ala Asp Tyr Asn Leu Thr Arg Ile Arg Pro Asp Cys Phe Leu  
340 345 350

Glu Val Ala Asp Glu Ala Thr Gly Ala Leu Ala Ser Ala Val Ser Gly  
355 360 365

Tyr Val Gln Ala Leu Ala Ser Ala Gly Val Val Ala Val Leu Ala Leu  
370 375 380

Gly Ala Pro Ala Pro Gln Gly Cys Ala Val Ala Leu Ala Ser Asp Arg  
385 390 395 400

Cys Ser Ile His Leu Gln Leu Gln Gly Leu Val Asp Pro Ala Arg Glu  
405 410 415

Leu Gly Lys Leu Gln Ala Lys Arg Val Glu Ala Gln Arg Gln Ala Gln  
420 425 430

Arg Leu Arg Glu Arg Arg Ala Ala Ser Gly Tyr Pro Val Lys Val Pro  
435 440 445

Leu Glu Val Gln Glu Ala Asp Glu Ala Lys Leu Gln Gln Thr Glu Ala  
450 455 460

Glu Leu Arg Lys Val Asp Glu Ala Ile Ala Leu Phe Gln Lys Met Leu  
465 470 475 480

&lt;210&gt; 560

517

&lt;211&gt; 96

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 560

Ala Cys Leu Glu Arg Cys Gly Ser Trp Arg Pro His Arg Pro Met Thr  
1 5 10 15

Ser Gly Ala Arg Glu Asn Pro Ile Gln Val Pro Arg Ser Ser Leu Glu  
20 25 30

Ala Thr Gly Ala Gln Glu Arg Trp Ala Glu Asp Val Pro Tyr Pro Thr  
35 40 45

Thr Arg Ala Val Ser Leu Pro Pro Ser Leu Gly Val Gly Ser Thr Gly  
50 55 60

Met Ser Ser Ser Arg Phe Leu Gly Ser Leu Gly Lys His Gly Arg Leu  
65 70 75 80

Asp Ser Ser Arg Arg Ala Arg Leu Trp Gly Arg Gly Gly Arg Gly Gly  
85 90 95

&lt;210&gt; 561

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 561

Ile Arg His Glu Ser Ser Ile Leu Ser Val Leu Phe Ile Arg Phe Leu  
1 5 10 15

Lys Cys Ala Asp Pro Phe Lys Thr Pro Ala Tyr Leu Cys Asn Lys Glu  
20 25 30

Lys Tyr Ser Lys Ile Leu Pro Ser Phe Ser His Thr Val Leu Lys Met  
35 40 45

Leu Gln Asp Gln Ile Ile Ala His Lys Ile Arg Ser  
50 55 60

&lt;210&gt; 562

&lt;211&gt; 241

&lt;212&gt; PRT

518

&lt;213&gt; Homo sapiens

&lt;400&gt; 562

```

Ser Ser Met Ala Lys Pro Cys Gly Val Arg Leu Ser Gly Glu Ala Arg
 1           5           10           15

Lys Gln Val Glu Val Phe Arg Gln Asn Leu Phe Gln Glu Ala Glu Glu
      20           25           30

Phe Leu Tyr Arg Phe Leu Pro Gln Lys Ile Ile Tyr Leu Asn Gln Leu
 35           40           45

Leu Gln Glu Asp Ser Leu Asn Val Ala Asp Leu Thr Ser Leu Arg Ala
 50           55           60

Pro Leu Asp Ile Pro Ile Pro Asp Pro Pro Pro Lys Asp Asp Glu Met
 65           70           75           80

Glu Thr Asp Lys Gln Glu Lys Lys Glu Val Pro Lys Cys Gly Phe Leu
      85           90           95

Pro Gly Asn Glu Lys Val Leu Ser Leu Leu Ala Leu Val Lys Pro Glu
      100           105           110

Val Trp Thr Leu Lys Glu Lys Cys Ile Leu Val Ile Thr Trp Ile Gln
      115           120           125

His Leu Ile Pro Lys Ile Glu Asp Gly Asn Asp Phe Gly Val Ala Ile
      130           135           140

Gln Glu Lys Val Leu Glu Arg Val Asn Ala Val Lys Thr Lys Val Glu
      145           150           155           160

Ala Phe Gln Thr Thr Ile Ser Lys Tyr Phe Ser Glu Arg Gly Asp Ala
      165           170           175

Val Ala Lys Ala Ser Lys Glu Thr His Val Met Asp Tyr Arg Ala Leu
      180           185           190

Val His Glu Arg Asp Glu Ala Ala Tyr Gly Glu Leu Arg Ala Met Val
      195           200           205

Leu Asp Leu Arg Ala Phe Tyr Ala Glu Leu Tyr His Ile Ile Ser Ser
      210           215           220

Asn Leu Glu Lys Ile Val Asn Pro Lys Gly Glu Glu Lys Pro Ser Met
      225           230           235           240

Tyr

```

519

<210> 563  
 <211> 200  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (145)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 563

Leu	Gly	Ser	Ile	Gln	Val	Met	Gln	Ala	Val	Arg	Asn	Ala	Gly	Ser	Arg	1	5	10	15
Phe	Leu	Arg	Ser	Trp	Thr	Trp	Pro	Gln	Thr	Ala	Gly	Arg	Val	Val	Ala	20	25	30	
Arg	Thr	Pro	Ala	Gly	Thr	Ile	Cys	Thr	Gly	Ala	Arg	Gln	Leu	Gln	Asp	35	40	45	
Ala	Ala	Ala	Lys	Gln	Lys	Val	Glu	Gln	Asn	Ala	Ala	Pro	Ser	His	Thr	50	55	60	
Lys	Phe	Ser	Ile	Tyr	Pro	Pro	Ile	Pro	Gly	Glu	Glu	Ser	Ser	Leu	Arg	65	70	75	80
Trp	Ala	Gly	Lys	Lys	Phe	Glu	Glu	Ile	Pro	Ile	Ala	His	Ile	Lys	Ala	85	90	95	
Ser	His	Asn	Asn	Thr	Gln	Ile	Gln	Val	Val	Ser	Ala	Ser	Asn	Glu	Pro	100	105	110	
Leu	Ala	Phe	Ala	Ser	Cys	Gly	Thr	Glu	Gly	Phe	Arg	Asn	Ala	Lys	Lys	115	120	125	
Gly	Thr	Gly	Ile	Ala	Ala	Gln	Thr	Ala	Gly	Ile	Ala	Ala	Ala	Ala	Arg	130	135	140	
Xaa	Lys	Gln	Lys	Gly	Val	Ile	His	Ile	Arg	Val	Val	Val	Lys	Gly	Leu	145	150	155	160
Gly	Pro	Gly	Arg	Leu	Ser	Ala	Met	His	Gly	Leu	Ile	Met	Gly	Gly	Leu	165	170	175	
Glu	Val	Ile	Ser	Ile	Thr	Asp	Asn	Thr	Pro	Ile	Pro	His	Asn	Gly	Cys	180	185	190	
Arg	Pro	Arg	Lys	Ala	Arg	Lys	Leu	195	200										

520

&lt;210&gt; 564

&lt;211&gt; 115

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 564

Val Arg Leu Val Pro Gly Ala Asp Lys Tyr Asn Asp Asp Ile Arg Lys  
 1 5 10 15

Gly Ile Val Leu Leu Glu Glu Leu Leu Pro Lys Gly Ser Lys Glu Glu  
 20 25 30

Gln Arg Asp Tyr Val Phe Tyr Leu Ala Val Gly Asn Tyr Arg Leu Lys  
 35 40 45

Glu Tyr Glu Lys Ala Leu Lys Tyr Val Arg Gly Leu Leu Gln Thr Glu  
 50 55 60

Pro Gln Asn Asn Gln Ala Lys Glu Leu Glu Arg Leu Ile Asp Lys Ala  
 65 70 75 80

Met Lys Lys Asp Gly Leu Val Gly Met Ala Ile Val Gly Gly Met Ala  
 85 90 95

Leu Gly Val Ala Gly Leu Ala Gly Leu Ile Gly Leu Ala Val Ser Lys  
 100 105 110

Ser Lys Ser  
 115

&lt;210&gt; 565

&lt;211&gt; 101

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 565

Pro Thr Arg Pro Asp Glu His Asp Glu Asn Asn Ala Glu Ala Ser Ala  
 1 5 10 15

Glu Leu Ser Asn Glu Gly Val Met Asn His Arg Ser Glu Glu Glu Arg  
 20 25 30

Val Thr Glu Thr Gln Lys Asn Glu Arg Val Lys Lys Gln Leu Gln Ala  
 35 40 45

Leu Ser Ser Glu Leu Ala Gln Ala Arg Asp Glu Thr Lys Lys Thr Gln

521

50                      55                      60  
 Asn Asp Val Leu His Ala Glu Asn Val Lys Ala Gly Arg Asp Lys Tyr  
 65                      70                      75                      80  
 Lys Thr Leu Arg Gln Ile Arg Gln Gly Asn Thr Lys Gln Arg Ile Asp  
                     85                      90                      95  
 Glu Phe Glu Ala Met  
                     100

<210> 566  
 <211> 25  
 <212> PRT  
 <213> Homo sapiens

<400> 566  
 Thr Ala Asp Leu Val Ile Arg Pro Pro Arg Pro Leu Lys Val Leu Gly  
 1                      5                      10                      15  
 Phe Cys Val Phe Cys Ala Pro Pro Leu  
                     20                      25

<210> 567  
 <211> 274  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (182)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (216)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (222)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (224)  
 <223> Xaa equals any of the naturally occurring L-amino acids

522

$\langle 220 \rangle$

<221> SITE

<222> (228)

```
<222> (228)
<223> Xaa equals any of the naturally occurring L-amino acids
```

<220>

<221> SITE

$\langle 222 \rangle$  (231)

```
<222> (231)
<223> xaa equals any of the naturally occurring L-amino acids
```

<400> 567

<400> 567  
Ala Ser Pro Glu Val Glu Ala Gly Ala Ala Arg Gln Pro Leu Leu Gly  
1 5 10 15

Val Ala Gly Gly Gln Thr Leu Gly Ala Thr Pro Gly Pro Val Met Asn  
20 25 30

Gly Pro Ala Asp Gly Glu Val Asp Tyr Lys Lys Lys Tyr Arg Asn Leu  
35 40 45

Lys Arg Lys Leu Lys Phe Leu Ile Tyr Glu His Glu Cys Phe Gln Glu  
50 55 60

Glu Leu Arg Lys Ala Gln Arg Lys Leu Leu Lys Val Ser Arg Asp Lys  
65 70 75 80

Ser Phe Leu Leu Asp Arg Leu Leu Gln Tyr Glu Asn Val Asp Glu Asp  
85 90 95

Ser Ser Asp Ser Asp Ala Thr Ala Ser Ser Asp Asn Ser Glu Thr Glu  
100 105 110

Gly Thr Pro Lys Leu Ser Asp Thr Pro Ala Pro Lys Arg Lys Arg Ser  
115 120 125

Pro Pro Leu Gly Gly Ala Pro Ser Pro Ser Ser Leu Ser Leu Pro Pro  
130 135 140

Ser Thr Gly Phe Pro Leu Gln Ala Ser Gly Val Pro Ser Pro Tyr Leu  
145 150 155 160

Ser Ser Leu Ala Ser Ser Arg Tyr Pro Pro Phe Pro Ser Asp Tyr Leu  
165 170 175

Ala Leu Gln Leu Pro Xaa Pro Ser Pro Leu Arg Pro Lys Arg Glu Lys  
180 185 190

Arg Pro Arg Leu Pro Arg Lys Leu Lys Met Ala Val Gly Pro Pro Asp  
195 200 205



523

Cys Pro Val Gly Gly Pro Leu Xaa Phe Pro Gly Arg Gly Xaa Gly Xaa  
210 215 220

Gly Val Gly Xaa Thr Leu Xaa Pro Leu Pro Pro Pro Lys Met Pro Pro  
225 230 235 240

Pro Thr Ile Leu Ser Thr Val Pro Arg Gln Met Phe Ser Asp Ala Gly  
245 250 255

Ser Gly Asp Asp Ala Leu Asp Gly Asp Asp Asp Leu Val Ile Asp Ile  
260 265 270

Pro Glu

<210> 568

<211> 133

<212> PRT

<213> Homo sapiens

**<220>**

**<221> SITE**

**<222> (47)**

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 568

Ala Arg Gly Asp His Val Arg Ser Arg Glu Thr Gly Arg Gln Ser Ala  
1 5 10 15

Ser Lys Gly Gln Ile Pro Leu Leu Pro Arg Gly Pro Ala Val Pro Gly  
20 25 30

Gly Pro Ser Ala Gln Thr Ala Ala Gln Arg Glu Leu Arg Gly Xaa Val  
35 40 45

Gly Ala Gly Ala Pro Val Tyr Leu Ala Ala Val Leu Glu Tyr Leu Thr  
50 55 60

Ala Glu Ile Leu Glu Leu Ala Gly Asn Ala Ala Arg Asp Asn Lys Lys  
65 70 75 80

Thr Arg Ile Ile Pro Arg His Leu Gln Leu Ala Ile Arg Asn Asp Glu  
85 90 95

Glu Leu Asn Lys Leu Leu Gly Lys Val Thr Ile Ala Gln Gly Gly Val  
100 105 110

Leu Pro Asn Ile Gln Ala Val Leu Leu Pro Lys Lys Thr Glu Ser Gln  
115 120 125

524

Lys Thr Lys Ser Lys  
130

<210> 569  
<211> 153  
<212> PRT  
<213> Homo sapiens

<220>  
<221> SITE  
<222> (136)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (137)  
<223> Xaa equals any of the naturally occurring L-amino acids

<220>  
<221> SITE  
<222> (152)  
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 569  
Met Cys Arg Gly Tyr Ala Trp Asn Pro Gly Ile Thr Leu Gln Asn Arg  
1 5 10 15  
Lys Thr Lys Glu Gly Pro Arg Ala Pro Pro Ser Arg Met Pro Glu Pro  
20 25 30  
Ala Gly Gly Leu Arg Gly Cys Glu Ala Val Gly Thr Leu Leu Met Lys  
35 40 45  
Glu Thr Val Phe Ala Leu His Pro Ser Leu Pro Leu Gly Ala Gly Ser  
50 55 60  
Ser Pro Ser Ala Thr Cys Ser Glu Gly Leu His Leu Arg Gly Glu Gly  
65 70 75 80  
Trp Gly Lys Ser Pro Pro Val Pro Phe Leu Trp Pro Cys Cys Pro His  
85 90 95  
Thr Gln Leu Arg Gly Pro Thr Leu Gly Lys Ala Gly Ser Ala Arg Ser  
100 105 110  
Leu Ser Pro Ile Ser Ala Leu Ser Ala Trp Ile Pro Ala Glu Ala Met  
115 120 125

525

Lys Gly Asn Lys Glu Lys Arg Xaa Xaa Lys Lys Lys Lys Lys Lys Lys  
 130 135 140

Lys Lys Lys Lys Lys Lys Lys Xaa Pro  
 145 150

<210> 570

<211> 327

<212> PRT

<213> Homo sapiens

<400> 570

Pro Gly Ser Pro Arg Arg Cys Asp Ile Ile Ile Ile Ser Gly Arg Lys  
 1 5 10 15

Glu Lys Cys Glu Ala Ala Lys Glu Ala Leu Glu Ala Leu Val Pro Val  
 20 25 30

Thr Ile Glu Val Glu Val Pro Phe Asp Leu His Arg Tyr Val Ile Gly  
 35 40 45

Gln Lys Gly Ser Gly Ile Arg Lys Met Met Asp Glu Phe Glu Val Asn  
 50 55 60

Ile His Val Pro Ala Pro Glu Leu Gln Ser Asp Ile Ile Ala Ile Thr  
 65 70 75 80

Gly Leu Ala Ala Asn Leu Asp Arg Ala Lys Ala Gly Leu Leu Glu Arg  
 85 90 95

Val Lys Glu Leu Gln Ala Glu Gln Glu Asp Arg Ala Leu Arg Ser Phe  
 100 105 110

Lys Leu Ser Val Thr Val Asp Pro Lys Tyr His Pro Lys Ile Ile Gly  
 115 120 125

Arg Lys Gly Ala Val Ile Thr Gln Ile Arg Leu Glu His Asp Val Asn  
 130 135 140

Ile Gln Phe Pro Asp Lys Asp Asp Gly Asn Gln Pro Gln Asp Gln Ile  
 145 150 155 160

Thr Ile Thr Gly Tyr Glu Lys Asn Thr Glu Ala Ala Arg Asp Ala Ile  
 165 170 175

Leu Arg Ile Val Gly Glu Leu Glu Gln Met Val Ser Glu Asp Val Pro  
 180 185 190

Leu Asp His Arg Val His Ala Arg Ile Ile Gly Ala Arg Gly Lys Ala

526

195	200	205
Ile Arg Lys Ile Met Asp Glu Phe Lys Val Asp Ile Arg Phe Pro Gln		
210	215	220
Ser Gly Ala Pro Asp Pro Asn Cys Val Thr Val Thr Gly Leu Pro Glu		
225	230	235 240
Asn Val Glu Glu Ala Ile Asp His Ile Leu Asn Leu Glu Glu Glu Tyr		
245	250	255
Leu Ala Asp Val Val Asp Ser Glu Ala Leu Gln Val Tyr Met Lys Pro		
260	265	270
Pro Ala His Glu Glu Ala Lys Ala Pro Ser Arg Gly Phe Val Val Arg		
275	280	285
Asp Ala Pro Trp Thr Ala Ser Ser Ser Glu Lys Ala Pro Asp Met Ser		
290	295	300
Ser Ser Glu Glu Phe Pro Ser Phe Gly Ala Gln Val Ala Pro Lys Thr		
305	310	315 320
Leu Pro Trp Gly Pro Lys Arg		
325		

&lt;210&gt; 571

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (9)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (12)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 571

Gly Asn Ser Arg Val Asp Pro Arg Xaa Arg Gly Xaa Ala His Thr Cys
1 5 10 15

Ala Pro Cys Pro Ala Pro Gly Pro Leu Ala Gly Arg Ala Val Ser Gly
20 25 30

His Gly Ser Leu Pro Pro Asp Arg Arg Ala Pro Ser Ala Leu Ser Ser

527

35                      40                      45  
 Pro Ala Asp Glu Gly Glu Arg Arg Arg Pro Asp Leu Asp Glu Ile His  
 50                      55                      60  
 Arg Glu Leu Arg Pro Gln Gly Ser Ala Arg Pro Gln Pro Asp Pro Asn  
 65                      70                      75                      80  
 Ala Glu Phe Asp Pro Asp Leu Pro Gly Gly Gly Leu His Arg Cys Leu  
 85                      90                      95  
 Ala Cys Ala Arg Tyr Phe Ile Asp Ser Thr Asn Leu Lys Thr His Phe  
 100                      105                      110  
 Arg Ser Lys Asp His Lys Lys Arg Leu Lys Gln Leu Ser Val Glu Pro  
 115                      120                      125  
 Tyr Ser Gln Glu Glu Ala Glu Arg Ala Ala Gly Met Gly Ser Tyr Val  
 130                      135                      140  
 Pro Pro Arg Arg Leu Ala Val Pro Thr Glu Val Ser Thr Glu Val Pro  
 145                      150                      155                      160  
 Glu Met Asp Thr Ser Thr  
 165

&lt;210&gt; 572

&lt;211&gt; 113

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 572

Gln Ser Ser Thr Phe His Pro Ala Pro Ala Phe Gly Ala Thr Val Ala  
 1                      5                      10                      15  
 Ala Phe His Arg Arg Ala Ala Leu Arg Ala Pro Glu Pro Ala Met Ser  
 20                      25                      30  
 Gly Pro Asn Gly Asp Leu Gly Met Pro Val Glu Ala Gly Ala Glu Gly  
 35                      40                      45  
 Glu Glu Asp Gly Phe Gly Glu Ala Glu Tyr Ala Ala Ile Asn Ser Met  
 50                      55                      60  
 Leu Asp Gln Ile Asn Ser Cys Leu Asp His Leu Glu Glu Lys Asn Asp  
 65                      70                      75                      80  
 His Leu His Ala Arg Leu Gln Glu Leu Leu Glu Ser Asn Arg Gln Thr  
 85                      90                      95

528

Arg Leu Glu Phe Gln Gln Gln Leu Gly Glu Ala Pro Ser Asp Ala Ser  
                   100                  105                  110

Pro

&lt;210&gt; 573

&lt;211&gt; 99

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (27)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (37)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (38)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 573

Gly Ser Gly Ser Ser Arg Asp Leu His Lys Ala Leu Trp Glu Ala Gly  
   1                  5                  10                  15

Trp Glu Thr Val Glu Gly Gly Cys Pro Leu Xaa Pro Arg Arg His Arg  
                   20                  25                  30

Ile Trp Ala Leu Xaa Xaa Ala Phe Leu Pro Glu Tyr Ala Ala Ile Asn  
                   35                  40                  45

Ser Met Leu Asp Gln Ile Asn Ser Cys Leu Asp His Leu Glu Glu Lys  
                   50                  55                  60

Asn Asp His Leu His Ala Arg Leu Gln Glu Leu Leu Glu Ser Asn Arg  
   65                  70                  75                  80

Gln Thr Arg Leu Glu Phe Gln Gln Gln Leu Gly Glu Ala Pro Ser Asp  
                   85                  90                  95

Ala Ser Pro

529

<210> 574  
 <211> 197  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (97)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (124)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (129)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 574  
 Arg Trp Ala Arg Val Glu Ala Ala Val Met Glu Gly Ala Gly Ala Gly  
     1                    5                    10                    15

Ser Gly Phe Arg Lys Glu Leu Val Ser Arg Leu Leu His Leu His Phe  
           20                    25                    30

Lys Asp Asp Lys Thr Lys Val Ser Gly Asp Ala Leu Gln Leu Met Val  
       35                    40                    45

Glu Leu Leu Lys Val Phe Val Val Glu Ala Ala Val Arg Gly Val Arg  
       50                    55                    60

Gln Ala Gln Ala Glu Asp Ala Leu Arg Val Asp Val Asp Gln Leu Glu  
       65                    70                    75                    80

Lys Val Leu Arg Ser Cys Ser Gly Leu Leu Gly Ile Ser Ala Val Ala  
           85                    90                    95

Xaa Ala Thr Pro Arg Gly Ala Pro Gly Pro Gln Lys Gln Ala Leu Cys  
           100                    105                    110

Phe Gln Arg Pro Leu Ile Arg Gly Arg Glu Gly Xaa Glu Gly Phe Gly  
       115                    120                    125

Xaa Asp Ser Asn Lys Ile Ser Gly Ser Leu Gln Pro Val Gln Lys Gly  
       130                    135                    140

Gln Asp Cys Ser Ala Leu Arg Ala Leu Glu Cys Pro Val Gly Thr Leu

530

145                      150                      155                      160  
 Val Trp Glu Gly Ala Ala Pro Gly Glu Ser Leu Pro Leu Leu Pro Gly  
                                  165                      170                      175  
 Thr Ile Val Cys Met Pro Pro Gly Val Leu Gln Ala Gly Ala Gly Lys  
                                  180                      185                      190  
 Gly Leu Ala Ser Arg  
                                  195

<210> 575  
 <211> 47  
 <212> PRT  
 <213> Homo sapiens

<400> 575  
 Leu Pro Met Val Asp Leu Met Glu Lys Leu Asn Ile Phe His Tyr Ala  
   1                                 5                                 10                                 15  
 Leu Gln Asn Thr Val Tyr Val Ser Ala Ser Leu Gly Asn Gly Arg Gly  
                                  20                                 25                                 30  
 Gln Lys Lys Val Thr Phe Asn Leu Cys Ile Phe Ala Lys Pro Tyr  
                                  35                                 40                                 45

<210> 576  
 <211> 115  
 <212> PRT  
 <213> Homo sapiens

<400> 576  
 Trp Ser Arg Thr Ser Gln Pro Leu Pro Ser Thr Val Gly Cys Pro Arg  
   1                                 5                                 10                                 15  
 Arg Arg Gly Phe Lys Asp Phe Gln Arg Arg Ile Leu Val Ala Thr Asn  
                                  20                                 25                                 30  
 Leu Phe Gly Arg Gly Met Asp Ile Glu Arg Val Asn Ile Ala Phe Asn  
                                  35                                 40                                 45  
 Tyr Asp Met Pro Glu Asp Ser Asp Thr Tyr Leu His Arg Val Ala Arg  
                                  50                                 55                                 60  
 Ala Gly Arg Phe Gly Thr Lys Gly Leu Ala Ile Thr Phe Val Ser Asp  
   65                                 70                                 75                                 80



531

Glu Asn Asp Ala Lys Ile Leu Asn Asp Val Gln Asp Arg Phe Glu Val  
                     85                    90                    95

Asn Ile Ser Glu Leu Pro Asp Glu Ile Asp Ile Ser Ser Tyr Ile Glu  
                     100                    105                    110

Gln Thr Arg  
                     115

&lt;210&gt; 577

&lt;211&gt; 346

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (37)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 577

Val Thr Ser Cys Val Ala Leu Leu Pro Ala Arg Arg Met Thr Tyr Thr  
     1                    5                    10                    15

Thr Glu Thr Ala Leu Leu Asn Trp Ser Thr Cys Gln Met Val Leu Arg  
                     20                    25                    30

Gly Ala Glu Thr Xaa Gly Cys Val Ile Val Ser Ala Ala Lys Ala Gln  
                     35                    40                    45

Leu Leu Gln Cys Gln His His Pro Ala Trp Tyr Gly Asp Thr Leu Lys  
     50                    55                    60

Gln Lys Thr Ser Trp Thr Cys Leu Leu Asp Gly Met Gln Tyr Phe Ala  
     65                    70                    75                    80

Thr Thr Glu Ser Ser Pro Thr Glu Gln Asp Gly Arg Gln Leu Trp Leu  
                     85                    90                    95

Glu Val Lys Asn Ile Glu Glu His Arg Gln Arg Ser Leu Asp Ser Val  
                     100                    105                    110

Gln Glu Leu Met Glu Ser Gly Gln Ala Val Gly Gly Met Val Thr Thr  
     115                    120                    125

Thr Thr Asp Trp Asn Gln Pro Ala Glu Ala Gln Gln Ala Gln Gln Val  
     130                    135                    140

Gln Arg Ile Ile Ser Arg Cys Asn Cys Arg Met Tyr Tyr Ile Ser Tyr  
     145                    150                    155                    160

532

Ser His Asp Ile Asp Pro Glu Leu Ala Thr Gln Ile Lys Pro Pro Glu  
 165 170 175

Val Leu Glu Asn Gln Glu Lys Glu Asp Leu Leu Lys Lys Gln Glu Gly  
 180 185 190

Ala Val Asp Thr Phe Thr Leu Ile His His Glu Leu Glu Ile Ser Thr  
 195 200 205

Asn Pro Ala Gln Tyr Ala Met Ile Leu Asp Ile Val Asn Asn Leu Leu  
 210 215 220

Leu His Val Glu Pro Lys Arg Lys Glu His Ser Glu Lys Lys Gln Arg  
 225 230 235 240

Val Arg Phe Gln Leu Glu Ile Ser Ser Asn Pro Glu Glu Gln Arg Ser  
 245 250 255

Ser Ile Leu His Leu Gln Glu Ala Val Arg Gln His Val Ala Gln Ile  
 260 265 270

Arg Gln Leu Glu Lys Gln Met Tyr Ser Ile Met Lys Ser Leu Gln Asp  
 275 280 285

Asp Ser Lys Asn Glu Asn Leu Leu Asp Leu Asn Gln Lys Leu Gln Leu  
 290 295 300

Gln Leu Asn Gln Glu Lys Ala Asn Leu Gln Leu Glu Ser Glu Glu Leu  
 305 310 315 320

Asn Ile Leu Ile Arg Cys Phe Lys Asp Phe Gln Leu Gln Arg Ala Asn  
 325 330 335

Lys Met Glu Leu Arg Lys His Lys Lys Met  
 340 345

&lt;210&gt; 578

&lt;211&gt; 91

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 578

Arg His Glu Gly His Leu Gly Ser Gly Arg Asn Gly Gly Gly Ser Met  
 1 5 10 15

Asn Ala Pro Pro Ala Phe Glu Ser Phe Leu Leu Phe Glu Gly Glu Lys  
 20 25 30

533

Ile Thr Ile Asn Lys Asp Thr Lys Val Pro Asn Ala Cys Leu Phe Thr  
35 40 45

Ile Asn Lys Glu Asp His Thr Leu Gly Asn Ile Ile Lys Ser Arg Ala  
50 55 60

Cys Phe Pro Phe Ala Phe Cys Arg Asp Cys Gln Phe Pro Glu Ala Ser  
65 70 75 80

Pro Ala Thr Leu Pro Val Gln Pro Ala Glu Leu  
85 90

&lt;210&gt; 579

&lt;211&gt; 331

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (18)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (20)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (300)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (311)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (313)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (320)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

534

&lt;222&gt; (325)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 579

Gly Arg Pro Thr Arg Pro Gly Gly Leu Gly Ser Gly Val Leu Ala Leu  
 1 5 10 15

Ala Xaa Gly Xaa Pro Ala Arg Leu Ala Gly Thr Val His Glu Val Gly  
 20 25 30

Asp Ala Pro Arg Arg Ala Pro Asp Gln Ala Ala Glu Ile Gly Ser Arg  
 35 40 45

Gly Ser Thr Lys Ala Gln Gly Pro Gln Gln Gln Pro Gly Ser Glu Gly  
 50 55 60

Pro Ser Tyr Ala Lys Lys Val Ala Leu Trp Leu Ala Gly Leu Leu Gly  
 65 70 75 80

Ala Gly Gly Thr Val Ser Val Val Tyr Ile Phe Gly Asn Asn Pro Val  
 85 90 95

Asp Glu Asn Gly Ala Lys Ile Pro Asp Glu Phe Asp Asn Asp Pro Ile  
 100 105 110

Leu Val Gln Gln Leu Arg Arg Thr Tyr Lys Tyr Phe Lys Asp Tyr Arg  
 115 120 125

Gln Met Ile Ile Glu Pro Thr Ser Pro Cys Leu Leu Pro Asp Pro Leu  
 130 135 140

Gln Glu Pro Tyr Tyr Gln Pro Pro Tyr Thr Leu Val Leu Glu Leu Thr  
 145 150 155 160

Gly Val Leu Leu His Pro Glu Trp Ser Leu Ala Thr Gly Trp Arg Phe  
 165 170 175

Lys Lys Arg Pro Gly Ile Glu Thr Leu Phe Gln Gln Leu Ala Pro Leu  
 180 185 190

Tyr Glu Ile Val Ile Phe Thr Ser Glu Thr Gly Met Thr Ala Phe Pro  
 195 200 205

Leu Ile Asp Ser Val Asp Pro His Gly Phe Ile Ser Tyr Arg Leu Phe  
 210 215 220

Arg Asp Ala Thr Arg Tyr Met Asp Gly His His Val Lys Asp Ile Ser  
 225 230 235 240

Cys Leu Asn Arg Asp Pro Ala Arg Val Val Val Val Asp Cys Lys Lys  
 245 250 255

535

Glu Ala Phe Arg Leu Gln Pro Tyr Asn Gly Val Ala Leu Arg Pro Trp  
260 265 270

Asp Gly Asn Ser Asp Asp Arg Val Leu Leu Asp Leu Ser Ala Phe Leu  
275 280 285

Lys Thr Ile Ala Leu Asn Gly Val Gly Gly Arg Xaa Glu Pro Cys Trp  
290 295 300

Glu His Tyr Ala Leu Gly Xaa Asp Xaa Pro Arg Trp Ala Ala Phe Xaa  
305 310 315 320

Asn Ser Gly Lys Xaa Gly Leu Glu Ala Gly Arg  
325 330

&lt;210&gt; 580

&lt;211&gt; 374

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (235)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (285)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (307)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (319)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (324)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (341)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (359)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 580

Pro Ser Thr Val Arg Asn Ser Arg Val Asp Pro Arg Val Arg Pro Arg  
1 5 10 15

Val Arg Ala Gly Val Ala Ala Leu Ala Thr Val Gly Val Ala Ser Gly  
20 25 30

Pro Gly Pro Gly Arg Pro Gly Pro Leu Gln Asp Glu Thr Leu Gly Val  
35 40 45

Ala Ser Val Pro Ser Gln Trp Arg Ala Val Gln Gly Ile Arg Gly Glu  
50 55 60

Thr Lys Ser Cys Gln Thr Ala Ser Ile Ala Thr Ala Ser Ala Ser Ala  
65 70 75 80

Gln Ala Arg Asn His Val Asp Ala Gln Val Gln Thr Glu Ala Pro Val  
85 90 95

Pro Val Ser Val Gln Pro Pro Ser Gln Tyr Asp Ile Pro Arg Leu Ala  
100 105 110

Ala Phe Leu Arg Arg Val Glu Ala Met Val Ile Arg Glu Leu Asn Lys  
115 120 125

Asn Trp Gln Ser His Ala Phe Asp Gly Phe Glu Val Asn Trp Thr Glu  
130 135 140

Gln Gln Gln Met Val Ser Cys Leu Tyr Thr Leu Gly Tyr Pro Pro Ala  
145 150 155 160

Gln Ala Gln Gly Leu His Val Thr Ser Ile Ser Trp Asn Ser Thr Gly  
165 170 175

Ser Val Val Ala Cys Ala Tyr Gly Arg Leu Asp His Gly Asp Trp Ser  
180 185 190

Thr Leu Lys Ser Phe Val Cys Ala Trp Asn Leu Asp Arg Arg Asp Leu  
195 200 205

Arg Pro Gln Gln Pro Ser Ala Val Val Glu Val Pro Ser Ala Val Leu  
210 215 220

Cys Leu Ala Phe His Pro Thr Gln Pro Ser Xaa Val Ala Gly Gly Leu

537

225                      230                      235                      240  
 Tyr Ser Gly Glu Val Leu Val Trp Asp Leu Ser Arg Leu Glu Asp Pro  
                                  245                      250                      255  
 Leu Leu Trp Arg Thr Gly Leu Thr Asp Asp Thr His Thr Asp Pro Val  
                                  260                      265                      270  
 Ser Gln Val Val Trp Leu Pro Glu Pro Gly His Ser Xaa Arg Phe Gln  
                                  275                      280                      285  
 Val Leu Ser Val Ala Thr Asp Gly Lys Val Leu Leu Trp Gln Gly Ile  
                                  290                      295                      300  
 Gly Val Xaa Gln Leu Gln Phe Thr Glu Gly Phe Ala Trp Phe Xaa Gln  
 305                                   310                      315                      320  
 Gln Leu Pro Xaa Ser Thr Lys Leu Lys Lys His Pro Arg Gly Arg Pro  
                                  325                      330                      335  
 Arg Trp Ala Pro Xaa Gln Ala Phe Phe Gln Phe Asp Leu Arg Phe Ser  
                                  340                      345                      350  
 Phe Trp Gln Glu Ala Val Xaa Val Gln Phe Ser Trp His Trp Arg Ala  
                                  355                      360                      365  
 Ala Leu Arg Gly Ala His  
                                  370

&lt;210&gt; 581

&lt;211&gt; 94

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (80)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (90)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 581

Cys Pro Asp Gln Asn Gly Trp Ala Ser Phe Gly Ala Pro Leu Ser Ala  
 1                      5                      10                      15

Gly Gly Gln Pro Cys Tyr Leu Leu Asp Ile Gly Cys Gly Ser Gly Leu

538

20                      25                      30  
 Ser Gly Asp Tyr Leu Ser Asp Glu Gly His Tyr Trp Val Gly Ile Asp  
                     35                      40                      45  
 Ile Ser Pro Ala Met Leu Asp Ala Ala Leu Asp Arg Asp Thr Glu Gly  
                     50                      55                      60  
 Asp Leu Leu Leu Gly Asp Met Gly Gln Gly Ile Pro Phe Lys Pro Xaa  
                     65                      70                      75                      80  
 Ser Leu Met Asp Val Ser Ala Phe Cys Xaa Ser Val Ala Leu  
                     85                      90

<210> 582  
 <211> 163  
 <212> PRT  
 <213> Homo sapiens

<400> 582  
 Pro Thr Arg Pro Ala Ala Gly Gly Ala Glu Arg Ile Ala Gly Ser Ala  
                     1                      5                      10                      15  
 Met Ser Ser Glu Pro Pro Pro Pro Pro Gln Pro Pro Thr His Gln Ala  
                     20                      25                      30  
 Ser Val Gly Leu Leu Asp Thr Pro Arg Ser Arg Glu Arg Ser Pro Ser  
                     35                      40                      45  
 Pro Leu Arg Gly Asn Val Val Pro Ser Pro Leu Pro Thr Arg Arg Thr  
                     50                      55                      60  
 Arg Thr Phe Ser Ala Thr Val Arg Ala Ser Gln Gly Pro Val Tyr Lys  
                     65                      70                      75                      80  
 Gly Val Cys Lys Cys Phe Cys Arg Ser Lys Gly His Gly Phe Ile Thr  
                     85                      90                      95  
 Pro Ala Asp Gly Gly Pro Asp Ile Phe Leu His Ile Ser Asp Val Glu  
                     100                      105                      110  
 Gly Glu Tyr Val Pro Val Glu Gly Asp Glu Val Thr Tyr Lys Met Cys  
                     115                      120                      125  
 Ser Ile Pro Pro Lys Asn Glu Lys Leu Gln Ala Val Glu Val Val Ile  
                     130                      135                      140  
 Thr His Leu Ala Pro Gly Thr Lys His Glu Thr Trp Ser Gly His Val  
                     145                      150                      155                      160



Ile Ser Ser

<210> 583  
 <211> 293  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (52)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (53)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (58)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (150)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (171)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (207)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (254)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 583  
 Leu Leu Gly Pro Asn Leu Thr Met Gly Ser Gln Pro Gly Arg Ile Pro  
       1                  5                  10                  15

Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr

540

	20		25		30
Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met Ile Asp Ser Glu					
	35		40		45
Cys Arg Pro Xaa Xaa Arg Glu Leu Val Xaa Glu Phe Ser Arg Met Ala					
	50		55		60
Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu Asp Leu Gly Pro					
	65		70		75
Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp					
		85		90	95
Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu Val Pro Gln Gln					
	100		105		110
Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly Gly Met Val His					
	115		120		125
His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly Gly Asp Leu Thr					
	130		135		140
Leu Gly Leu Glu Pro Xaa Glu Arg Gly Gly Pro Gln Val Ser Thr Gly					
	145		150		155
Thr Leu Arg Arg Ala Gly Ser Asp Val Phe Xaa Gly Asp Leu Gly Met					
		165		170	175
Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His Asp Pro Ser Pro					
	180		185		190
Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu Pro Ser Xaa Thr					
	195		200		205
Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val					
	210		215		220
Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro					
	225		230		235
Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Xaa Lys Thr					
		245		250	255
Leu Ser Pro Gly Lys Asn Gly Val Val Lys Glu Phe Leu Pro Leu Gly					
	260		265		270
Val Pro Trp Arg Thr Pro Ser Ile Asp Thr Pro Gly Glu Gly Ala Cys					
	275		280		285
Pro Ser Ala Pro Pro					

541

290

&lt;210&gt; 584

&lt;211&gt; 132

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 584

Gly Gly Ala Gln Pro Gly Met Glu Gly Ala Ala Thr Val His Leu  
 1 5 10 15

Ile Ser Gln Trp Ala Val Glu Pro Asn Ala Arg Val Gly Pro Leu Leu  
 20 25 30

Glu Val Glu Ala Ala Ala Ala Asp His His Glu Ala Ala Ala Gly Ala  
 35 40 45

Gly Ser Ala Val Glu Lys Ile Cys Ile Asp Lys Gly Leu Thr Asp Glu  
 50 55 60

Ser Glu Ile Leu Arg Phe Leu Gln His Gly Thr Leu Val Gly Leu Leu  
 65 70 75 80

Pro Val Pro His Pro Ile Leu Ile Arg Lys Tyr Gln Ala Asn Ser Gly  
 85 90 95

Thr Ala Met Trp Phe Arg Thr Tyr Met Trp Gly Val Ile Tyr Leu Arg  
 100 105 110

Asn Val Asp Pro Pro Val Trp Tyr Asp Thr Asp Val Lys Leu Phe Glu  
 115 120 125

Ile Gln Arg Val  
 130

&lt;210&gt; 585

&lt;211&gt; 218

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (54)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (92)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (117)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (140)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (141)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (188)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (199)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (200)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 585

Arg	Glu	Arg	Cys	Arg	Arg	Glu	Ala	Leu	Arg	Gly	Ser	Arg	Leu	Cys	Pro
1				5					10					15	

Ala	Thr	Pro	Pro	Ser	Ala	Leu	Gly	Ser	Gln	Asp	Gly	Ser	Arg	Thr	Arg
				20				25					30		

Asp	Arg	Leu	Gly	Ala	Ala	Gly	Trp	Pro	Gly	Leu	Val	Val	Gly	Leu	Cys
		35					40					45			

Thr	Pro	Ala	Ala	Gly	Xaa	Gln	Arg	Asp	Leu	Leu	His	Arg	Arg	Gly	Gly
		50				55					60				

Thr	Ala	Ser	Phe	Gly	Lys	Ser	Phe	Ala	Gln	Lys	Ser	Gly	Tyr	Phe	Leu
	65				70					75					80

Cys	Leu	Ser	Ser	Leu	Gly	Ser	Leu	Glu	Asn	Pro	Xaa	Glu	Asn	Val	Val
				85					90					95	

543

Ala Asp Ile Gln Ile Val Val Asp Lys Ser Pro Leu Pro Leu Gly Phe  
                   100                  105                  110

Ser Pro Val Cys Xaa Pro Met Asp Ser Lys Ala Ser Val Ser Lys Lys  
                   115                  120                  125

Lys Arg Met Cys Val Lys Leu Leu Pro Leu Gly Xaa Xaa Asp Thr Ala  
                   130                  135                  140

Val Phe Asp Val Arg Leu Ser Gly Lys Thr Lys Thr Val Pro Gly Tyr  
                   145                  150                  155                  160

Leu Arg Ile Gly Asp Met Gly Gly Phe Ala Ile Trp Cys Lys Lys Gly  
                   165                  170                  175

Gln Gly Pro Glu Ala Ser Cys Pro Lys Pro Arg Xaa Pro Gln Pro Gly  
                   180                  185                  190

Thr Cys Lys Gly Phe Ser Xaa Xaa Ala Ala Ser Gln Pro Lys Leu Arg  
                   195                  200                  205

Ala Gly Leu Leu Gly Ser Arg Thr Ser Val  
                   210                  215

&lt;210&gt; 586

&lt;211&gt; 233

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (41)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 586

Ala Arg Gly Glu Met Glu Gly Arg Gln Val Leu Glu Val Lys Met Gln  
   1                  5                  10                  15

Val Glu Tyr Met Ser Phe Ser Ala His Ala Asp Ala Lys Gly Ile Met  
                   20                  25                  30

Gln Leu Val Gly Gln Ala Glu Pro Xaa Ser Val Leu Leu Val His Gly  
                   35                  40                  45

Glu Ala Lys Lys Met Glu Phe Leu Lys Gln Lys Ile Glu Gln Glu Leu  
                   50                  55                  60

Arg Val Asn Cys Tyr Met Pro Ala Asn Gly Glu Thr Val Thr Leu Pro

544

[illegible]

<210> 587

<211> 116

<212> PRT

<213> Homo sapiens

**<220>**

<221> SITE

$\langle 222 \rangle$  (100)

```
<222> (100)
<223> Xaa equals any of the naturally occurring L-amino acids
```

<400> 587

Gly Pro Leu Ser His His Ile Arg Ala Gln Leu Ser Lys Met Leu Leu  
1 5 10 15

Ala Arg Lys Gln Ile Leu Cys Val Asn Val Lys Asn Phe Ala Val Ile  
20 25 30

```
Tyr Leu Val Asp Ile Thr Glu Val Pro Asp Phe Asn Lys Met Tyr Glu
      35                      40                      45

Leu Tyr Asp Pro Cys Thr Val Met Phe Phe Phe Arg Asn Lys His Ile
      50                      55                      60

Met Ile Asp Leu Gly Thr Gly Asn Asn Asn Lys Ile Asn Trp Ala Met
      65                      70                      75                      80

Glu Asp Lys Gln Glu Met Val Asp Ile Ile Glu Thr Val Tyr Arg Gly
              85                      90                      95

Ala Arg Lys Xaa Arg Gly Leu Val Val Ser Pro Lys Asp Tyr Ser Thr
          100                      105                      110

Lys Tyr Arg Tyr
        115
```

```
<210> 588
<211> 133
<212> PRT
<213> Homo sapiens
```

```

<400> 588
Ala Arg Ala Ala Val Gly Arg Thr Ala Gly Val Arg Thr Trp Ala Pro
  1             5             10             15

Leu Ala Met Ala Ala Lys Val Asp Leu Ser Thr Ser Thr Asp Trp Lys
      20             25             30

Glu Ala Lys Ser Phe Leu Lys Gly Leu Ser Asp Lys Gln Arg Glu Glu
      35             40             45

His Tyr Phe Cys Lys Asp Phe Val Arg Leu Lys Lys Ile Pro Thr Trp
      50             55             60

Lys Glu Met Ala Lys Gly Val Ala Val Lys Val Glu Glu Pro Arg Tyr
      65             70             75             80

Lys Lys Asp Lys Gln Leu Asn Glu Lys Ile Ser Leu Leu Arg Ser Asp
      85             90             95

Ile Thr Lys Leu Glu Val Asp Ala Ile Val Asn Ala Ala Asn Ser Ser
      100             105             110

Pro Pro Pro Arg Ser Leu Ile Lys Asp Leu Arg Cys Gly Lys Lys Lys
      115             120             125

Lys Lys Lys Lys Lys

```

546

130

&lt;210&gt; 589

&lt;211&gt; 163

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 589

Arg His Arg Gly Gln Pro Leu Arg Gln Thr Arg Ala Ser Ser Ser Pro  
 1 5 10 15

Gln Leu Ala Gly Arg Ser Ser Ser Val Leu Pro Ala Ala Ala Gln Pro  
 20 25 30

Cys Thr Pro Thr Met Asp Val Phe Lys Lys Gly Phe Ser Ile Ala Lys  
 35 40 45

Glu Gly Val Val Gly Ala Val Glu Lys Thr Lys Gln Gly Val Thr Glu  
 50 55 60

Ala Ala Glu Lys Thr Lys Glu Gly Val Met Tyr Val Gly Ala Lys Thr  
 65 70 75 80

Lys Glu Asn Val Val Gln Ser Val Thr Ser Val Ala Glu Lys Thr Lys  
 85 90 95

Glu Gln Ala Asn Ala Val Ser Glu Ala Val Val Ser Ser Val Asn Thr  
 100 105 110

Val Ala Thr Lys Thr Val Glu Glu Ala Glu Asn Ile Ala Val Thr Ser  
 115 120 125

Gly Val Val Arg Lys Glu Asp Leu Arg Pro Ser Ala Pro Gln Gln Glu  
 130 135 140

Gly Glu Ala Ser Lys Glu Lys Glu Glu Val Ala Glu Glu Ala Gln Ser  
 145 150 155 160

Gly Gly Asp

&lt;210&gt; 590

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 590



547

Arg Ala Leu Leu Cys Leu Gly His His Pro Leu Leu Ala Gln Gly Val  
 1 5 10 15

Pro Ala Leu Ser Asp Met Arg Leu Pro Thr Leu Leu Pro Ser Ser Pro  
 20 25 30

Trp Pro Pro Leu Ala Cys Pro Pro Val Leu Leu His Gln Pro His Cys  
 35 40 45

Pro Pro Ser Ala Pro Pro Thr Leu Trp Ser Phe  
 50 55

<210> 591

<211> 116

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (31)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 591

Val His Ala Glu Ala Gly Arg Leu Cys His Gly Asp Cys Pro Arg Leu  
 1 5 10 15

Cys Arg Pro Arg Gln Arg Ser Ala Pro Val Gln Val Tyr Thr Xaa Arg  
 20 25 30

Gln Ala Ala Leu His Gly Arg Pro Gln Arg Asp Pro Cys Val Gly Gly  
 35 40 45

Pro Arg Pro Leu Arg Cys Ser Arg Asp Cys Gly Gly Gly His Gln Arg  
 50 55 60

Leu Val Met Pro Gly Thr Trp Thr Gln Ala Trp Gln Arg Arg Gln Val  
 65 70 75 80

Val Asn Gly Leu Met Leu Gly Gln Ala Arg Ile His Val Asn Arg Leu  
 85 90 95

Glu Gln Ala Val Val Asn Leu Ala Pro Cys Glu Tyr Phe His Thr Cys  
 100 105 110

Cys Pro Phe Ala  
 115

<210> 592  
 <211> 290  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> SITE  
 <222> (30)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>  
 <221> SITE  
 <222> (239)  
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 592  
 Arg Arg Ser Leu Asn Thr His Gly Ser Gly Val Ser Val Cys Leu Gln  
           1                  5                  10                  15  
 Ser Leu Thr Leu Leu Ala Thr Leu Cys Pro Gly Asp Gln Xaa Ser Leu  
                   20                  25                  30  
 Gly Leu Leu Thr Pro Cys Tyr Ser Gly Ser Glu Pro Ser Gly Thr Phe  
           35                  40                  45  
 Gly Pro Val Asn Pro Ser Leu Asn Asn Thr Tyr Glu Phe Met Ser Thr  
           50                  55                  60  
 Phe Phe Leu Glu Val Ser Ser Val Phe Pro Asp Phe Tyr Leu His Leu  
           65                  70                  75                  80  
 Gly Gly Asp Glu Val Asp Phe Thr Cys Trp Lys Ser Asn Pro Glu Ile  
                   85                  90                  95  
 Gln Asp Phe Met Arg Lys Lys Gly Phe Gly Glu Asp Phe Lys Gln Leu  
           100                  105                  110  
 Glu Ser Phe Tyr Ile Gln Thr Leu Leu Asp Ile Val Ser Ser Tyr Gly  
           115                  120                  125  
 Lys Gly Tyr val val Trp Gln Glu Val Phe Asp Asn Lys Val Lys Ile  
           130                  135                  140  
 Gln Pro Asp Thr Ile Ile Gln Val Trp Arg Glu Asp Ile Pro Val Asn  
           145                  150                  155                  160  
 Tyr Met Lys Glu Leu Glu Leu Val Thr Lys Ala Gly Phe Arg Ala Leu  
                   165                  170                  175  
 Leu Ser Ala Pro Trp Tyr Leu Asn Arg Ile Ser Tyr Gly Pro Asp Trp  
           180                  185                  190